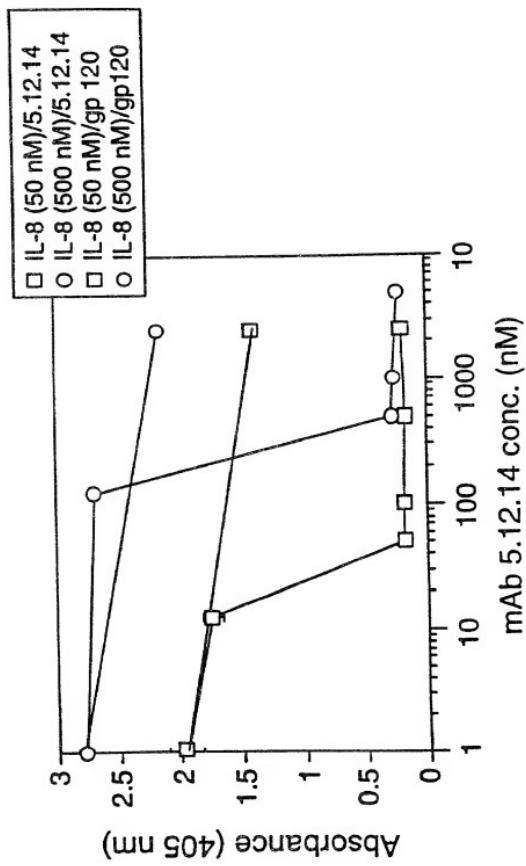
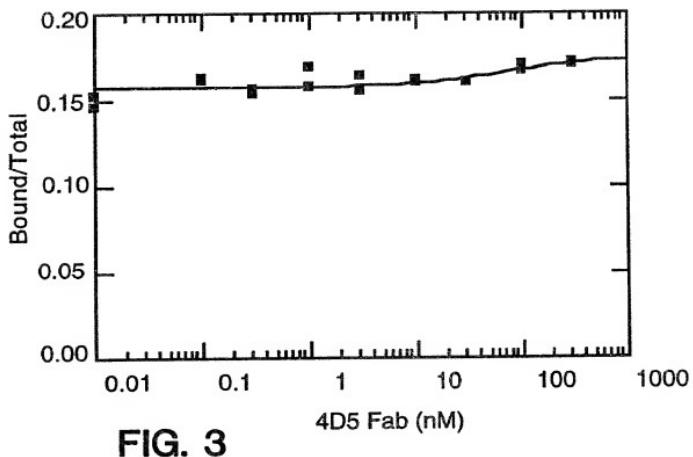
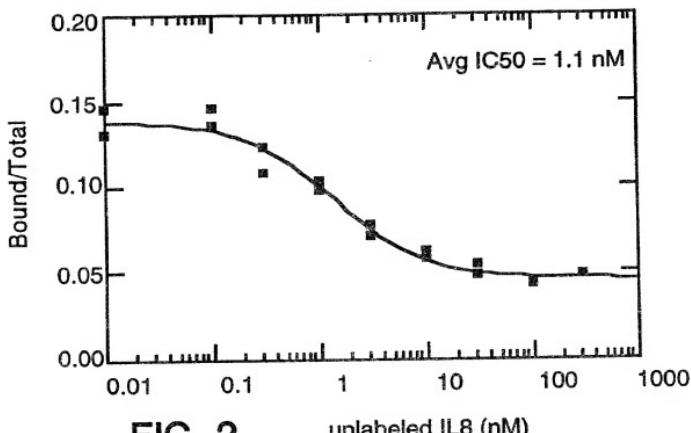


FIG. 1





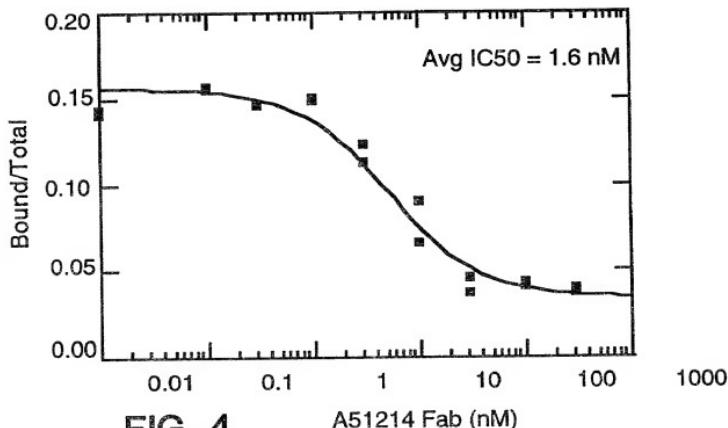


FIG. 4

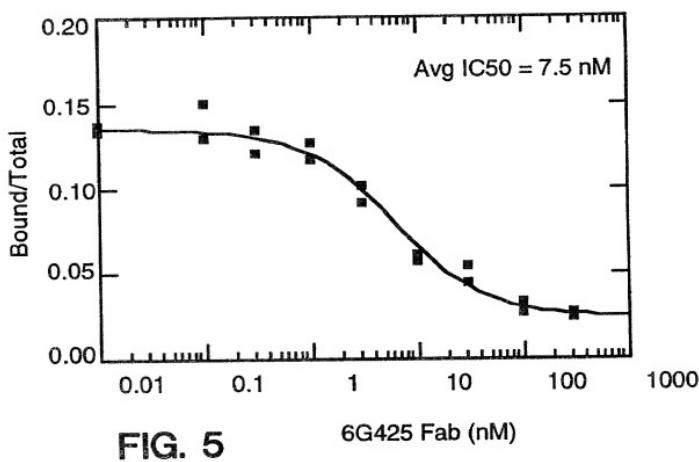


FIG. 5

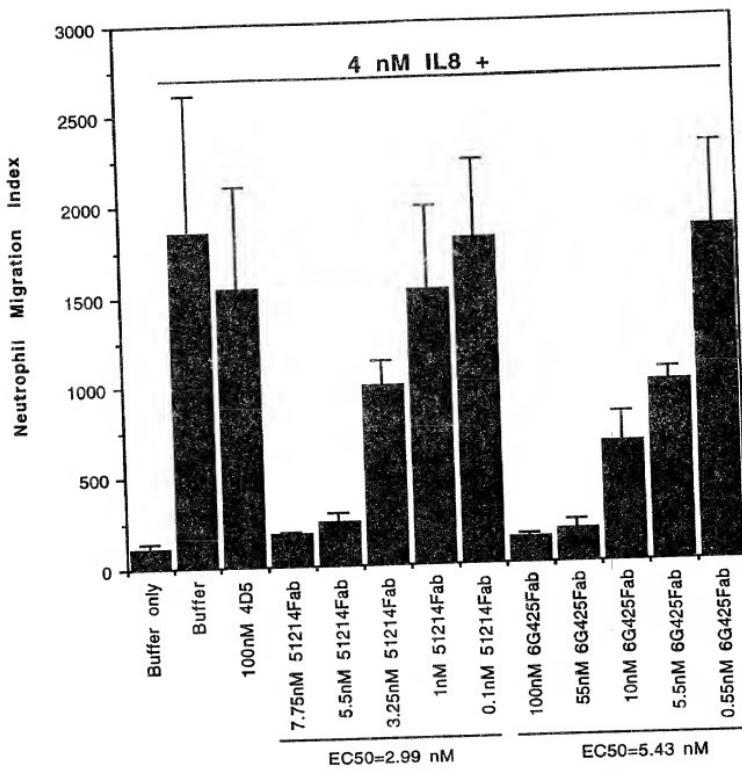


FIG. 6

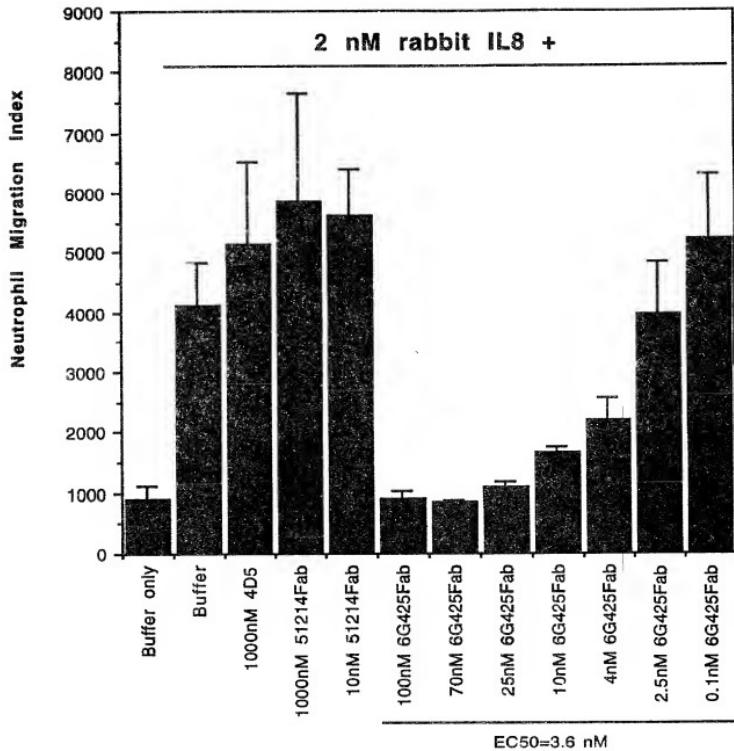


FIG. 7

FIG. 8

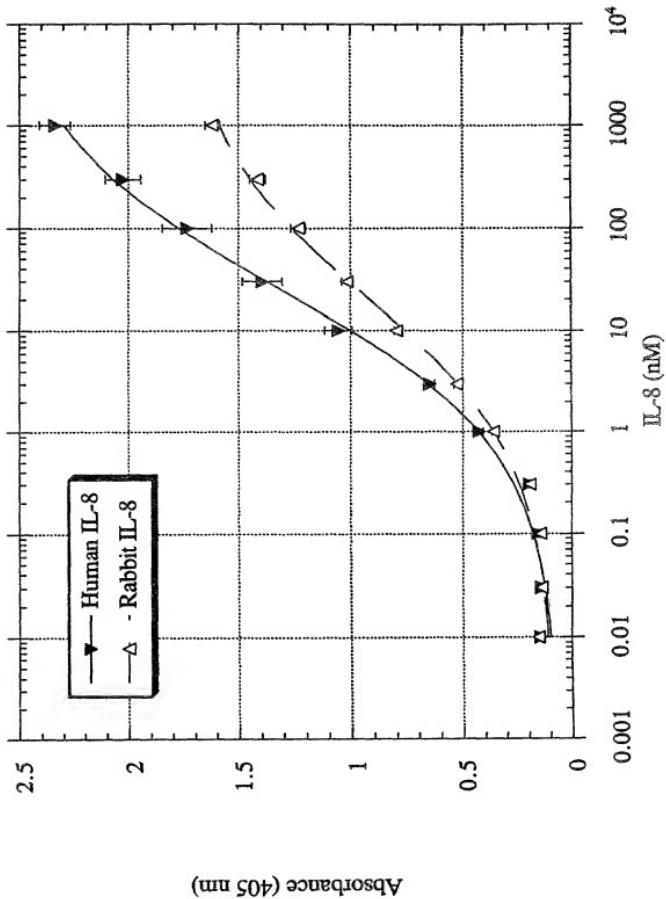


FIG. 9

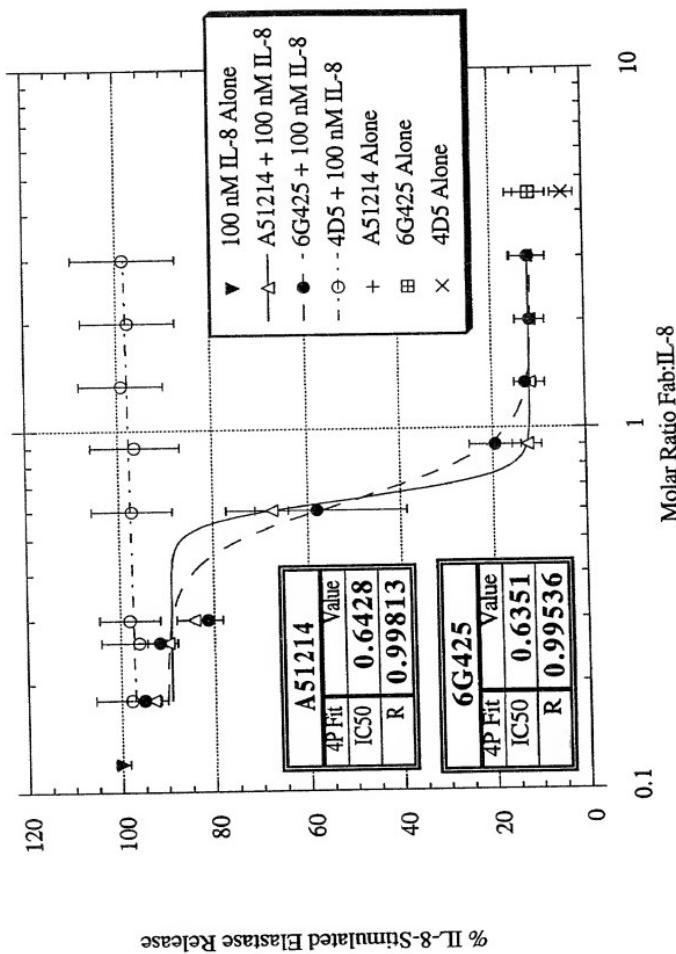
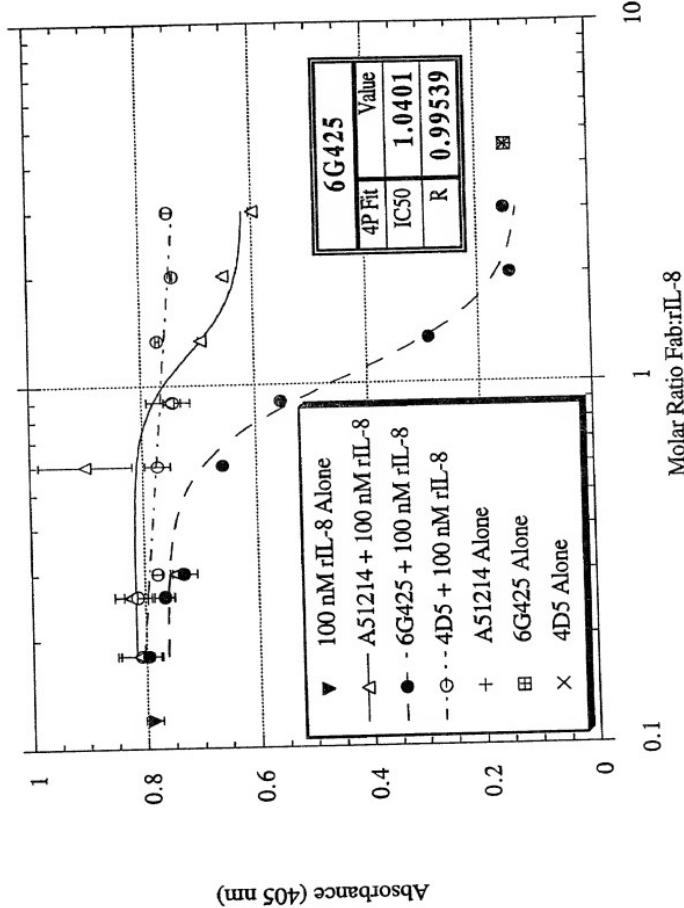


FIG. 10



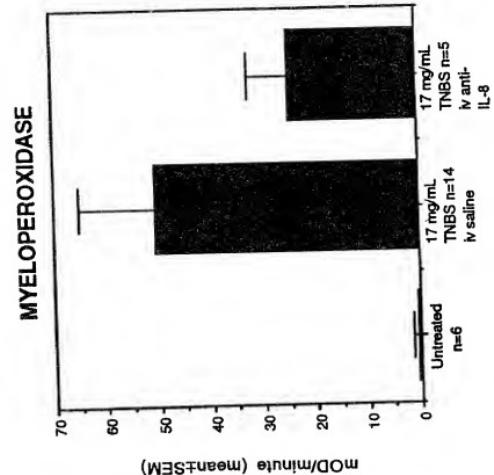


FIG. 11A

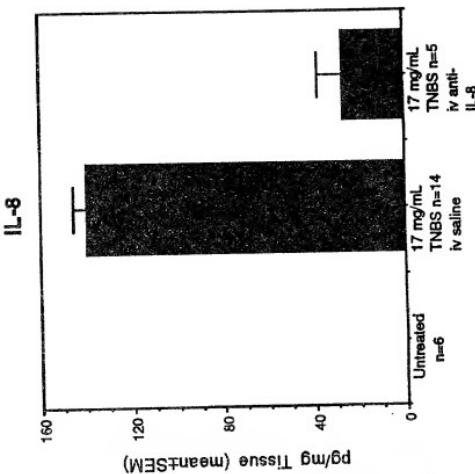


FIG. 11B

FIG. 11D

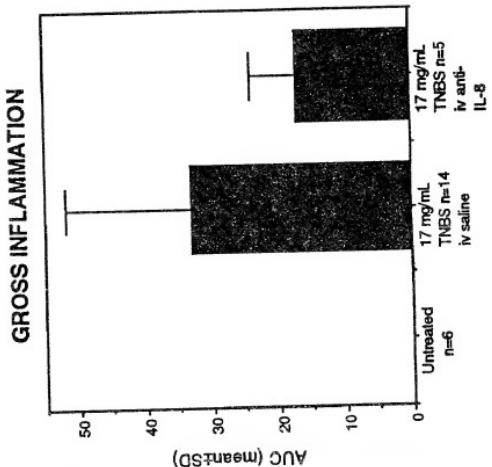


FIG. 11C

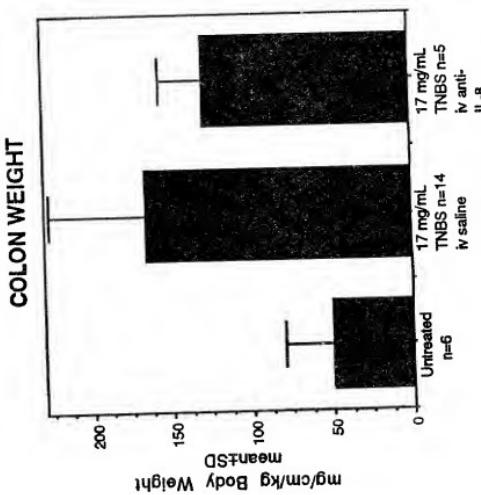


FIG. 11F

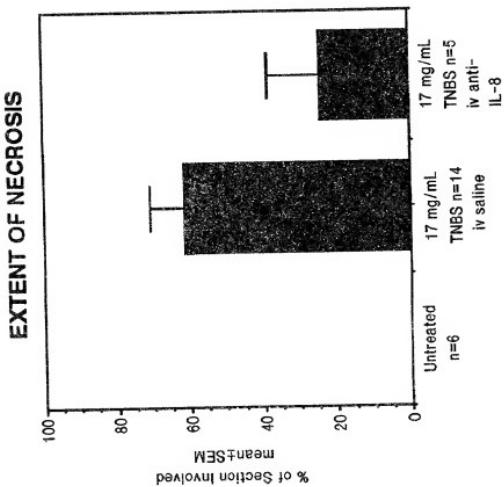
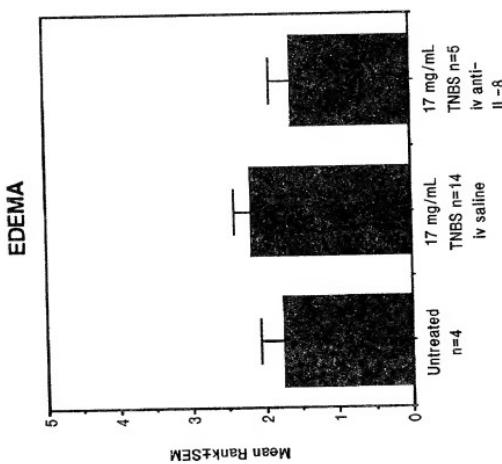


FIG. 11E



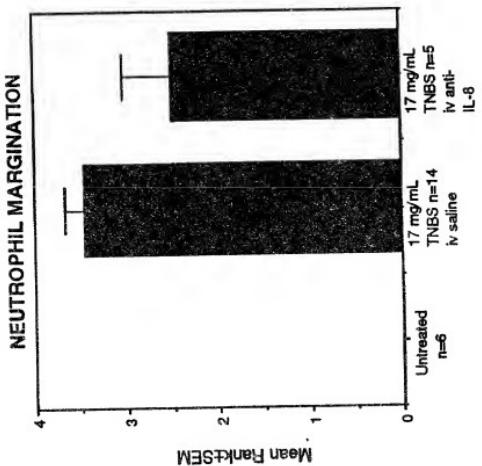


FIG. 11H

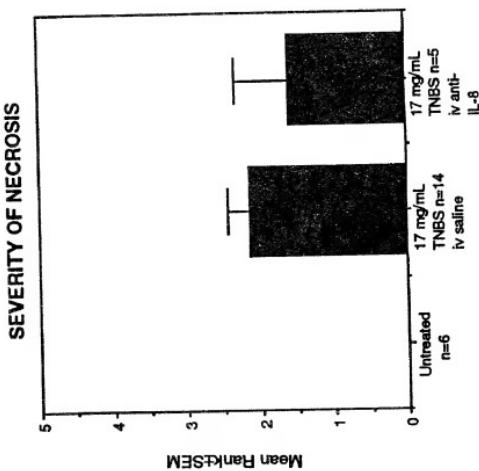


FIG. 11G

FIG. 11J

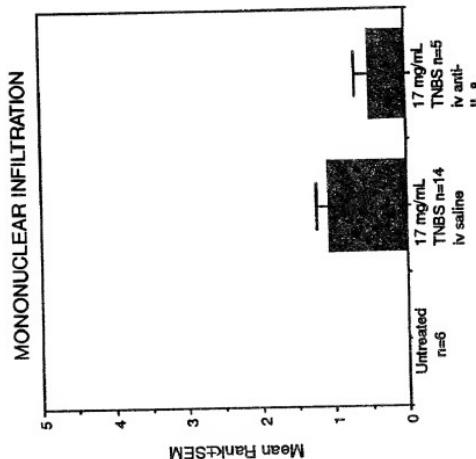


FIG. 11I

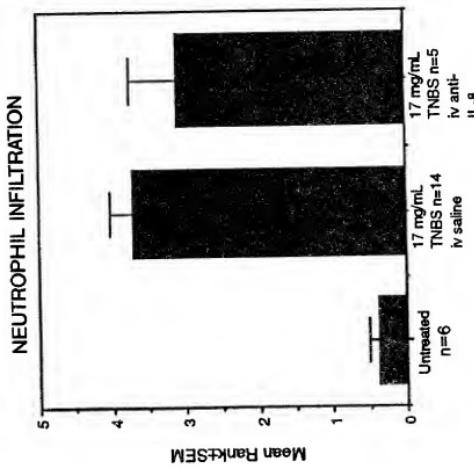
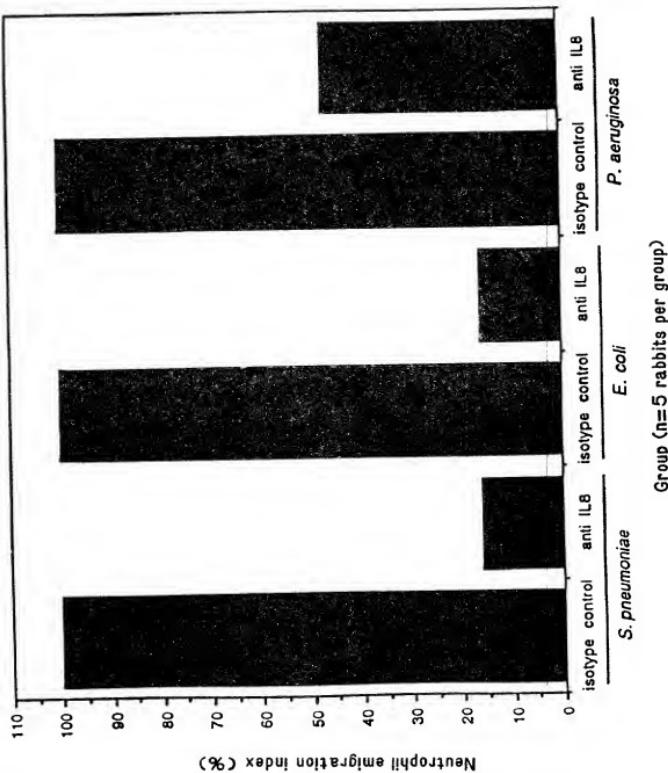


FIG. 12



Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCA ACTGTT CAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 13

FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGGTACGCT GACATCGTGTGACCCAGTC 3' (SEQ ID NO.7)
T T T T A
(SEQ ID NO.8) (SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGAAAGATGGATAACAGTTGGTGC 3' (SEQ ID NO.10)

卷之三

Heavy chain forward primer

SL002B 39 mer

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGCCGG ATAGACCGATGGGCTGTGTGTTGGC
 T A G
 (SEQ ID NO.11) (SEQ ID NO.15) (SEQ ID NO.14)
 (SEQ ID NO.13)

卷之三

1	GACATTGCA	TGACACAGTC	TCAAATTC	ATGTCACAT	CAGTAGGAA	CAGGCTCAGC
		CITGTAACGT	ACTGTGCA	AGTTTGTG	TACGGTGA	GTCCAGCTG
1	D	I	V	M	T	Q
	S	Q	K	F	M	S
	T	S	V	G	D	R
						S
51	GTCACGTGCA	AGGGCAAGTC	GAATGGGT	ACTAATGTTAG	CTCGGTATCA	ACGAAACCCA
		CAGTGACGT	TCCGGCAGT	CTTAACCCCA	TGATTAACATC	GGACCATAGT
						TGTCCTGGT
21	V	T	C	K	A	S
	*	*	*	*	*	O
	*	*	*	*	*	N
	*	*	*	*	*	V
	*	*	*	*	*	G
	*	*	*	*	*	T
	*	*	*	*	*	N
	*	*	*	*	*	V
	*	*	*	*	*	A
	*	*	*	*	*	W
	*	*	*	*	*	Y
	*	*	*	*	*	Q
	*	*	*	*	*	K
	*	*	*	*	*	P

CGCTTACAG	GCAGGGATC	TGGGACAGAT	TTCACTCTCA	CCATCAGCCA	TGTGGAGTC
CGAAATGTC	CCTCACTAG	ACCCGTC	AAGTGAGGT	GTTAGTCGGT	ACACGTCAGG
61 R F T G	S G S	G T D	F T L T	I S H V Q S	
GAAGCTTGG	CAGACTATT	CTGTCAGCAA	TATAAACATCT	ATCCTCTCAC	GTTCGCTCC
CTCTGAAAC	CTCTGATAAA	GACAGTGGT	ATATTGTAGA	TAGGAGTGT	CAAGGCCAGG
81 E D L A	D Y F C	Q Q	Y N I Y	P L T	F G P
	*	*	*	*	*

301	GGGACCAAGC	TGGAGTGTAA	ACGGGTGACCA	CAACTGTATC	CATCTCCCA
	CCCTGGTTCG	ACCTCAACTT	TGCCGACTA	CGACGTGGTG	GTRGAAGGGT
101	G T K L E	L K A D A	P P T V S	I F P	

BstBI
361 CCATTGCA
GGTAAGCT
121 P F E

361 CCATTGAA (SEQ ID NO.16)
362 CCTTCCCTT (SEQ ID NO.17)

16 FIG

1 TTCTATTCGCT ACAAACCGGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
 AGATAACGA TGTTTGCAC TGCACACTCA CGTCGACCAC CTCAAGACCC CTCCGAATCA
 1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCAATAT TCAGTAGTTA
 CGGGGACCT CCCAGGGACT TTGAGAGGAC ACAGTCGGAGA CCTAAGTATA AGTCATCAAT
 13 P P G G S S L K L S C A A S G F I F S S Y
 * * *

CDR #1

121 TGGCATGTCT TGGGTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTA
 ACCGTACAGA ACCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCGAC GTTGGTAATT
 33 G M S W V R Q T P G K S L E L V A T I N
 * * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCGGATTCA CCATCTCCG
 ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAAGT GGTAGAGGGC
 53 N N G D S T Y P D S V K G R F T I S R
 * * * * * * * * * * * * *

CDR #2

241 AGACAATGCC AAAAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
 TCTGTTACGG TTCTTGTGGG ACATGGACAGT TTACTCGTCA GACTTCAGAC TCCCTGTGCG
 73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTGGTT ACTGGGGCCA
 GTACAAAATG ACAGTCTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCCGGT
 93 M F Y C A R A L I S S A T W F G Y W G Q
 * * * * * * * * * * * *

CDR #3

361 AGGGACTCTG GTCACTGTCT CTGCAGCCAA AACAAACAGCC CCATCTGTCT
 TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCGG GGTAGACAGA
 113 G T L V T V S A A K T T A P S V Y

ApaI
 411 ATCCGGG (SEQ ID NO.18)
 TAGGCC (SEQ ID NO.19)
 130 P

FIG. 17

FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

O 5/26/2008 10:51:00 AM

1 ATGAGAAGAA ATATCGCATT TCTTCTTGCA TCTATGGTCG TTTTTCTAT TGCTACAAAC
 TACTCTCT TATAGCGTAA AGAAAGAACCT AGATACAAACG AAAAGAGATA ACAGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCGTACCGCT ATATCGCTAT GACACAGTC GAAAATTC A TGTCACATC AGTAGGGACAG
 CGCATGGCAC TATAGCGTAA CTGTGTCAGA GTTTTTAAGT ACAGGTGTTAG CATCCCTCTG
 -3 A Y A D I V M T Q S Q K F M S T S V G D

 121 AGGGTCACGG TCACCTGCAA GGCCAGTCG AATGTGGGTA CTAATGTAGC CTGGTATCAA
 TCCCAGTCG A GTGGACGTT CGGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
 18 R V S V T C K A S O N V G T N V A W Y Q
 * * * * * * * * * * * * * * * * * *
 CDR #1

 181 CAGAACCCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCCTACCG GTACAGTGGAA
 GTCTTTGGTC CGCGTTAGAGG ATTTCTGTC A TAAATGAGCA GTAGGATGGC CATGTCACCT
 38 Q K P G Q S P K A L I Y S S S Y R Y S G
 * * * * * * * * * * * * * * * * * *
 CDR #2

 241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCACCCAT
 CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTCTCTAA ACTGAGAGTG GTAGTCGGTA
 58 V P D R F T G S G S G T D F T L T I S H

 301 GTGCAGCTG AAGACTTGGC AGACTATTTC TGTCAGCAAT ATAACATCTA TCCTCTCACG
 CACOTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
 78 V Q S E D L A D Y F C Q Q Y N I Y P L T
 * * * * * * * * * * * * * * * * * *
 CDR #3
 BstBI

 361 TTGGTCTCTG GGACCAAGCT GGAGCTCTGA AGAGCTGTGG CTGACCCATC TGTCITCTAC
 AAGCCAGGAC CCTGGTCTGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
 98 F G P G T K L E L R R A V A A P S V F I

 421 TTCCCGCCAT CTGATGAGCA GTTGAATCTT GGAACGTCTT CTGTTGTGTG CCTGCTGAAT
 AAGGGCGGTA GACTACTGCT CAACCTTATAA CTTCTGAGCAA GACAACACAC GGACGACTTA
 118 F P P S D E Q L K S G T A S V W V C L L N

 481 AACTCTTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACCCCTT CCAATCTGGGT
 TTGAAAGATAG GGTCTCTCCG GTTTCATGTC ACCCTTCACC TATTGGGGG GTTAGGCCA
 138 N F Y P R E A K V Q W K V D N A L Q S G

 541 AACTCCCAAGG AGAGTGTCAAG AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
 TTGAGGGTCC TCTCACAGT TCTCGTCTG TGTTCTCTGT CGTGGATGTC GGAGTCGTC
 158 N S Q E S V T E Q D S K D S T Y S L S S

 601 ACCCTGAGCG TGAGCAAAGC AGACTACCG AGAACACAAAG TCTACGCCCT CGAACGTACCC
 TGGGACTCGG ACTCGTTTCG TCTGATGCTC TTGTTGTTTC AGATGGGGAC GCTTCAGTGG
 178 T L T L S K A D Y E K H K V Y A C E V T

 661 CATCAGGGCC TGAGCTCGG CGTCACAAAG AGCTTCACAA GGGGGAGAGTG
 GTAGTCGGG ACTCGAGGGC CGAGTGTTCG TGCAAGTTGT CCCCTCTCAC
 198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

FIG. 19

1 ATGAAAAAGA ATATCGCATT TCTTCITGCA TCTATGTTCG TTTTTCTAT TGCTACAAAC
 TACTTTTCT TATAGCGTAA AGAGAACGT AGATACAAAGC AAAAAGATA ACGATGTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCGTACCGTG AGGGAGCTG GTGGAGCTC GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
 CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCG ACCTCCCAGG
 -3 A Y A E V Q L V E S G G G L V P P G G S

 121 CTGAAACTCT CCTGTCGAGC CTCTGGATTC ATATTCAAGTA GTTATGGCAT GTCTTGGGT
 GACTTGGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCAA
 18 L K L S C A A S G F I F S S Y G M S W V
 * * * * * * *
 CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTGGCAACCA TTAATAATAA TGTTGATAGC
 GCGGCTGAG GTCCGTTCTC GGACCTAAC CAGCGTTGGT ATTATTATT ACCACTATCG
 38 R Q T P G K S L E L V A T I N N N G D S
 *

 241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
 TGGATAATAG GTCTGTCACA CTTCGGGT AAATGGTAGA GGGCTCTGTT ACGGTTCTTG
 58 T Y Y P D S V K G R F T I S R D N A K N
 * * * * * * * * * * *
 CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTCGA
 TGGGACATGG ACGGTTACTC GTCAAGACTTC AGACTCCTGT GTCGGTACAA ATGACACGTT
 78 T L Y L Q M S S L K S E D T A M F Y C A

 361 AGAGCCCTCA TTAGTTGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
 TCTCGGGAGT AATCAAGCCG ATGAACAAA CCAATGACCC CGGTTCCCTG AGACCACTGAA
 98 R A L I S S A T W F G Y W G Q G T L V T
 *
 CDR #3

ApAI

421 GTCTCTGCAG CCTCCACCAA GGCCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
 CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGGTCTCG
 118 V S A A S T K S P S V F P L A P S S K S

 481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAGG ACTACTTCCC CGAACCGGTG
 TGGAGACCCC CGTGTGCGCG GGACCCGACG GACCAAGTCC TGATGAAGGG GCTTGGCCAC
 138 T S G G T A A L G C L V K D Y F P E P V

 541 ACGGTGTCGT GGAACCTCAGG CGCCCTGACCC AGCGGCGTGC ACACCTTCCC GGCTGTCCCTA
 TGGCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCAAGC TGTGGAAGGG CCGACAGGAT
 158 T V S W N S G A L T S G V H T F P A V L

 601 CAGCTCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
 GTCAAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACAGGGAGGTC GTCGAACCCG
 178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCCGAGACCT ACATCTGCAA CGTGAAATCAC AAGCCGAGCA ACACCAAGGT GGACAGAGAA
198 TGGGTCCTCGGA TGTTAGACGTT GCACATTACTG TTCCGGTCTGT GTGTGTTCCA CCTGTATCCTT
198 T Q T Y I C N V N H K P S N T K V D K K
721 GTTGAGGCCA AATCTTGTGA CAAAACTCAC ACATGTA (SEQ ID NO.26)
218 V E P K S C D K T H T O (SEQ ID NO.27)
218 V E P K S C D K T H T O

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAAC TGTT CAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21

FIGURE 22

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATAAGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
T T T T
A A A A
(SEQ ID NO.28)
(SEQ ID NO.29)
(SEQ ID NO.30)

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'
(SEQ ID NO.31)

FIG. 22

FIG. 23

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGGCTAGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGCCCCGG ATAGACCGATGGGCCTGTTGTTGGC 3' (SEQ ID NO.11)
T A (SEQ ID NO.15)
A G (SEQ ID NO.14)
G (SEQ ID NO.13)

70 G ATATCGTGTAC GACACAGACA CCACCTCTCC TGCTGTCAG TCTTGAGAT
 C TATACCACTA CTGTGTCGTG GTGAGAGGG ACCGACAGTC AAACACTTA
 1 D I V M T Q T P L S V P S L G D

 121 CAGGCCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTGTAC ACGGTATTGG AAACACCTAT
 GTCGGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTGTTGGATA
 18 Q A S I S C R S S O S L V H G I G N T Y
 *
 CDR #1

 181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAGC TCCTGATCTA CAAAGTTCC
 AAATGTAACCA TGACCTCTT CGGTCGGTC AGAGGTTTCG AGGACTAGAT GTTCAAAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * * * * *
 CDR #2

 241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTCACAA
 TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * * * * *

 301 CTCAGGATCA GCAGAGTGG A GGCTGAGGAT CTGGGACTTT ATTCTGCTC TCAAAGTACA
 GAGTCTTAGT CGTCTCACCT CCGACTCCCTA GACCTGAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * * * * *
 CDR #3

 361 CATGTTCCG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
 GTACAAGGGC AGTGCAGGCC ACGACCCCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT
 98 H V P L T F G A G T K L E L K R A D A A
 * * * * * *
 MunI

 421 CCAACTGTAT CCATCTTCCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34)
 GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT
 118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24

70 G AGATTCTAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
 C TCTAATGTC CGTCGTCAG CCTGACTCG ACTACTTCGG ACCCGAAGT
 1 E I Q L Q Q S G P E L M K P G A S

 121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * * * * * * * * *
 CDR #1

181 AACGAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGTACACA TTGATCCTTC CAATGGTGA
 TTCGCTCTCGG TACCTTCTC GGAACCTACCC TAACCGATGT ACTAGGAAG GTTACCACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 *
 CDR #2

241 ACTACTTACA ACCAGAAAATT CAAGGGCAAG GCCACATTGA CTGTAGAACAC ATCTTCCAGC
 TGATGAATGT TGGTCTTAA GTTCCCCTTC CGGTGTAACCT GACATCTGTG TAGAACGTCG
 58 T T Y N Q K F K G K A T L T V D T S S S
 *
 CDR #3

301 ACAGCCAACG TGATCTCGAG CAGCCTGACA TCTGTAGACT CTGCACTCTA TTCTGTGCA
 TGTGGTTCG ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAAGAT AAACACACGT
 78 T A N V H L S S L T S D D S A V Y F C A
 *
 CDR #4

361 AGAGGGGACT ATAGATACAA CGGGCAGTGG TTTTCGATG TCTGGGGCGC AGGGACACCG
 TCTCCCTGAG TATCTATGTT GCGCTGACCC AAAAACCTAC AGACCCCCCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T
 *
 CDR #5

BstEII **ApAI**
 421 GTCACCGCTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGCC
 CAGTGGCAGA GGAGGGGGAT TTGGCTGTCG GGGTAGCCAG ATAGGCCGG
 118 V T V S S A K T D S P I G L S G P P

471 CATC (SEQ ID NO.36)
 GTAG

135 I (SEQ ID NO.37)

FIG. 25

5' CTTGGTGGAGGC GGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGC GGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

1 ATGAGAAGAATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTTCTAT TGCTACAAAT
 TACTTCTCT TATAGGTAA AGAAGAACGT AGATACAAGC AAAAAGATA ACGATGTTA
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCGTGAT GACACAGACA CCACCTCTCC TGCCCTGTCAG TCTTGGAGAT
 CGTATGGAC TATAGCACTA CTGTGTCCTGT GGTTGAGAGGG ACGGACAGTC AGAACCTCTA
 -3 A Y A D I V M T Q T P L S L P V S L G D

 121 CAGGCCCTCA TCTCTTGAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGAACATG TGCCATAACC TTGTTGAGATA
 18 Q A S I S C R S S O S L V H G I G N T Y
 *
 CDR #1

181 TTACATTGGT ACCTGAGAA GCCAGGGAG TCTCCAAGC TCCCTGATCTA CAAAGTTCC
 AAATGTAACCA TGGACGCTT CGGTCGGTC AGAGGTTCTG AGGACTAGAT GTTCAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * * * * *
 CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTTC AGTGGCAGTG GATCAGGGAC AGATTTACCA
 TTGGCTAAA GACCCAGGG TCTGTCAG TCAACGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * * * * *

301 CTCAGGATCA GCAGAGTGGGAGGAT CTGGGACTTT ATTCTGCTC TCAAAGTACA
 GAGTCTCTAGT CGCTCACCT CGCACTCCTA GACCTGAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * * * * *
 CDR #3

361 CATGTTCCGC TCACGTTGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTTGCTGCA
 GTACAAGGGCG AGTGAAGCC ACAGACCTGG TTCGACCTCG ACTTTGCCCG ACAACGACGT
 98 H V P L T F G A G T K L E L K R A V A A
 * * * * * * * *

421 CCAACTGTAT TCATCTTCCCC ACCATCCAGT GAGCAATTGA AATCTGGAAAC TGCCCTGTT
 GGTTGACATA AGTAGAAGGG TGTTAGGTCA CTCGTTAACT TTAGACCTTG ACGGAGACAA
 118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTTGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTAA GCCCCATTGAG GTCCCTCTCA CAGTGTCTCG TCCGTGCGTT CCTGTCGTTG
 158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGCTCTGA TGCTCTTGT GTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

661 GCCTGGAAAG TCACCCATCA GGGCCTGAGC TCGCCCTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGTAGT CCCGGACTCG AGCGGGAGT GTTTCTCGAA GTGTGCCCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAA (SEQ ID NO.41)
CTGACGATT (SEQ ID NO.42)
218 E C O

FIG. 27B

1 ATGAAAAAGA ATATCCGATT TCTTCTTGCA TCTATGTTCG TTTTTCTAT TGCTACAAAC
 TACTTTTCT TATAGCGTAA AGAAAACGT AGATACAAGC AAAAAGATA ACGATGTTG
 -23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTCAAGCT GCACCGAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTC
 CGCATGGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCGAAGT
 -3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAAGCCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * * *

CDR #1

181 AAGCACAGGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCCTC CAATGGTGA
 TTCGCTCTGG TACCTTCTC GGAACTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 * * * * * * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
 TGATGAATGT TGGCTTTAA GTTCCCGTTC CGGTGTAACACT GACATCTGTG TAGAAGGTCG
 58 T T Y N Q K F K G K A T L T V D T S S S
 * * * * * * * *

301 ACAGCCAACG TGCATCTCAAG CAGCGTGACA TCTGATGACT CTGCAGTCGA TTTCTGTGCA
 TGTCGGTGTG ACAGTAGAGTCG GTCCGACTGT AGACTACTGA GACGTCAGAT AAAGACAGT
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGACT ATAGATACAA CGGGCACTGG TTTCGATG TCTGGGGCGC AGGGACCACG
 TCTCCCTGA TATCTATGTT GCGCGTGCACC AAAAGCTAC AGACCCCGCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T T
 * * * * * * * * *

CDR #3

421 GTCACCGTCT CCTCCGCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCCTC
 CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
 118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGGGCCCTG GGTCGCTGG TCAAGGACTA CTTCCCCGAA
 TTCTCGTGGA GACCCCGCTG TCGCCGGAC CCGACGGACC AGTCCTGTAT GAAGGGCCTT
 138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCTGTGAA CTCAGGCAGCC CTGACCGAGCG GCGTGCACAC CTTCCCGGCT
 GGCCACTGCC ACAGCACCTT GAGTCGGCGG GACTGGTCGC CGCACCGTGT GAAGGGCCGA
 158 P V T V S W N S G A L T S G V H T F P A

601 GTCTTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCGC
 CAGGATGTCA GGAGTCTGA GATGAGGGAG TCCTCGCAC ACTGGCACGG GAGGTCGTG
 178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A

661 TTGGGCACCC AGACCTACAT CTGCCAACGTG AATCACAAAGC CCAAGCAACAC CAAGGTGGAC
AACCCCTGGG TCGGATATA GACGTTGCACT TAGTGTGTTG GTTCACACTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AGAAAGTTG AGCCAAATC TTGTGACAAA ACTCACACAT GA (SEQ ID NO.43)
TCTTTCAAC TCGGGTTAG AACACRGTTC TGAGTGTATA CT
218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B

Variable Light Chain Domain

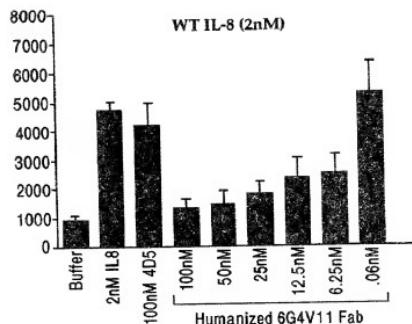
	10	20	abcde	30	40
6G425	DIVMTQTPLSLPVSLGDQASISCRSSQSLVHIGINTYLHWYLOKPGQQSPKLLIY				
F(ab)-1	DIQMTQSPSSLASAVGDRVTITCRSSQSLVHIGINTYLHWYQQKPGKAPKLLIY				
humκI	DIQMTQSPSSLASAVGDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY				
			=====		
			+++++		
				L1	
6G425	50 60 70 80 90 100	YKVSNRFSGVPDFRSQSGSGTDFTLR1S1RVEAEDLGLYFCQSHTHPLTFGAGTKLELKR	(SEQ ID NO.45)		
F(ab)-1	YKVSNRFSGVPSRFSQSGSGTDFTLTISSLQPEDFATYYCQSHTHPLTFGQGTKEIKR	(SEQ ID NO.46)			
humκI	YSGSTLSEGVPSRFSQSGSGTDFTLTISSLQPEDFATYYCQHNEYPLTFGQGTKEIKR	(SEQ ID NO.47)			
	====	=====			
	++++++	++++++			
	L2	L3			

Variable Heavy Chain Domain

	10	20	30	40	
6G425	EIQLQSQSPPELMKPGASVKISCKASGYSFSSHYMHWVKQSHGKSLWEI				
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMHWVRQAPGKGLEWV				
humIII	EVQLVESGGGLVQPGGSLRLSCAASGSPFTGHWMWVRQAPGKGLEWV				
	=====	=====			
	+++++	+++++			
		H1			
6G425	50 a 70 80 abc 90 100 110	GYIDPSNGETTYNQKFKGKATLTVDTSSSTANVHLSSLTSDDSAVYFCAAARGDYRYNGDWFFDVWQAGT	(SEQ ID NO.48)		
F(ab)-1	GYIDPSNGETTYNQKFGRFTISRDNISKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWQAGT	(SEQ ID NO.49)			
humIII	GMIIHPSDGETRAYDSVKGRFTISRDNISKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTYYFDWQAGT	(SEQ ID NO.50)			
	====	=====			
	++++++	++++++			
	H2	H3			

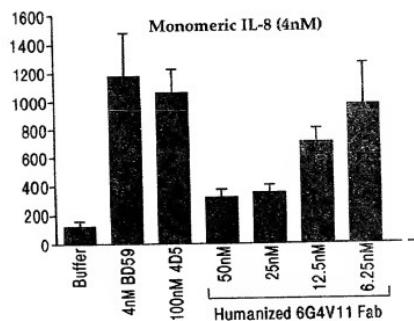
FIG. 29

FIG. 30A



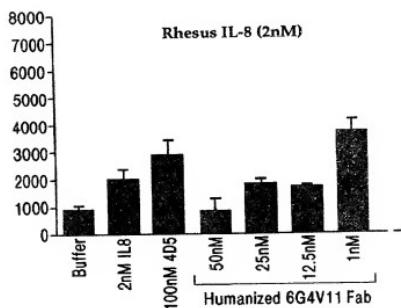
IC50~12nM

FIG. 30B



IC50~15nM

FIG. 30C



IC50~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNTIAFLLASMFVFSLATNAYAADIOMTQSPSSILSASVGDRVTITCRSSOSLVLHGIINTY
LHWYQOKPGKAPKLILYKVSNRFSGVPSRREFSGGSQGTDFTLTITISLQPEDFATYYCSQQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQRSGTASVCLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDTSTYSSLSTTLSKADYEHKRVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNTIAFLLASMFVFSLATNAYAAEVQLVQSGGLVQPGGSTRLSCAASGYFSSHYMH
WVRQAPGKGLEMWVGYIDPSNGETTYNQKFKGRTFLSRDNSTNTAVLQMNISLRAEDTAVYY
CARGDYRYNGDWFFDVMQGQTLYTVTSSASTKGPSVFLPAPSXKSTISGGTTAALGCLVKDIF
PEPYTVSNWSNGSALTSGVHTFPAVLQSSGGLYLSLSSVTVTPSSSLGTQTYICNVNHHKPNTK
VDKRYEPKSCCDRHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGSGDFDYEKMANANKGAMTENADENALQSDAKGKLDSTYATDYGAIDGFIGDVS
GLANGNGATGDPAGSSNSOMAQVGDGDNSPLMNNFROYLPSPQSYECRPFVFSAGKPY
EFSIDCDKTINLFRGVFAFLLYVATFMYVFSTFANILRNKES (SEQ ID NO.53)

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTTCTAT TGCTACAAAC
 TACTTTCT TATAGGGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CGCAGCTCC TGTCCGCCCTC TGTGGGCGAT
 CGTATCGCAC TATAGGTCTA CTGGGTCAAGG GGCTCGAGGG ACAGGGGGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCTA
 18 R V T I C T R S S Q S L V H G I G N T Y

 181 TTACACTGGT ATCAAACAGAA ACCAGGGAAA GCTCCGAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGCTT TGTCCTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
 TTAGCTAAGA GACCTCAGGG AAAGCGAAG AGACCTAGGC CAAGACCTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T

 301 CTGACCACATCA GCAGTCTGCA GCCAGAACAGC TTGCAACATT ATTACTGTT ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGTCTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
 78 L T I S S L Q P E D F A T Y Y C S Q S T

 361 CATGTCCCCG TCACGTTGG ACAGGGTACCA AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
 GTACAGGGCG AGTCAAACCC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

 421 CCATCTGCT TCATCTTCCC GGCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
 GGTAGACAGA AGTAGAACGG CGGTAGACTA CTCGTCACACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V

 481 GTGTGCTGC TGAATAACCTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
 CACACGGACG ACTTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATG
 138 V C L L N N F Y P R E A K V Q W K V D N

 541 GGCCTCCAAT CGGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTTA GCCCCATTGAG GTCTCTCTCA CAGTGTCTCG TCCGTGCTT CCTGTGCTGG
 158 A L Q S G N S Q E S V T E Q D S K D S T

 601 TACAGCCTCA GCAGCACCC GACGCTGAGC AAAGCAGACT ACGGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTTGGA CTGCGACTCG TTTCGCTGTA TGCTTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

 661 GCCTGCGAAG TCACCCATCA GGGCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC ACTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCCCT
 198 A C E V T H Q G L S S P V T K S F N R G
 (SEQ ID NO.54)
 721 GAGTGTAAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTACAATTC GACTAGGAGA TGCGGCCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
 218 E C O (SEQ ID NO.51)

FIG. 31B

FIGURE 3C 6G4.2.5V19

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLIASMFEVSSTATNAVADIONTQSPTPSLSASVGDRVTITCRSSQSLVHGLIGNY
LHWYQQKPGKAPKLITKVSNRFSGYPSRFSGSGSGTDFLTITISIOPEDFATYCQSOST
HVPLTFGGQTKEIKRTVAAPSVFIFPSDEQLKSGTASVVLNNFYPREAKVQNMVKDN
ALQSGNSQEVTEQDSKDSTYSLSLSSLTLSKADYERKHYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO:51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLIASMFEVSSTATNAVAEVOLVESGGGLVQPGESRLSCAAGYGSFSSHHVMH
WVKOAPGKGLEWVGYIDPSNGETYNQFKGFTLSRDNSKNTAYLOMNSURAEDTAVYY
CARGDYRYNGDMFFDWGQGTIVTVSSASTKGPSPVFLAPAPSXKSTSGGTAAALGCLVKDVF
PEPVTVSNNSGALTSGVETEPAPVLOSSGLYSLSVVTPSSSLGTQTYICVNHKPSNTK
VDRKVEPKSCDKTH (SEQ ID NO:55)

FIG. 3C

FIG. 32

Humanized Anti-IL8 Antibody

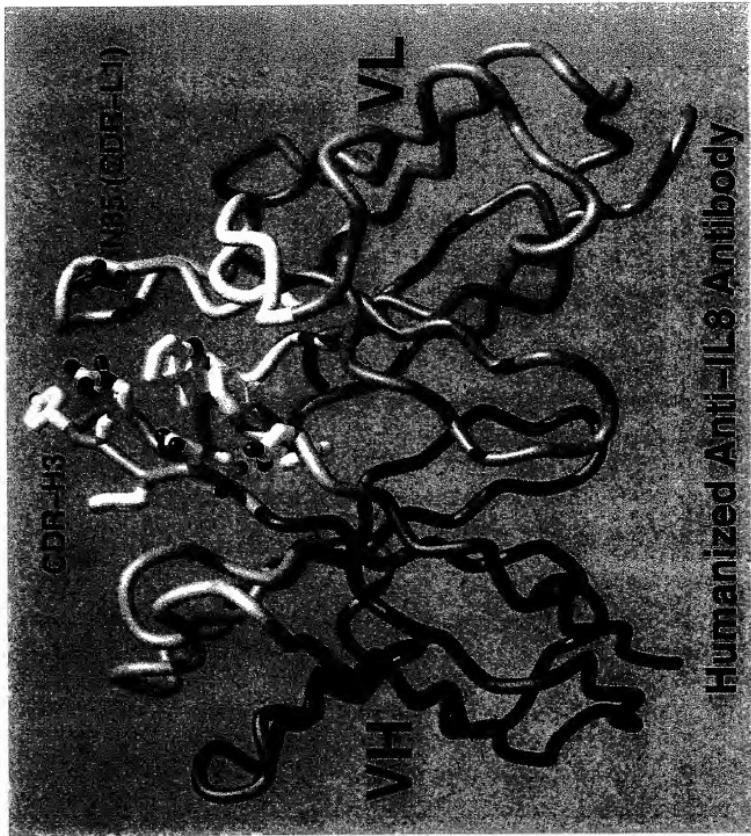
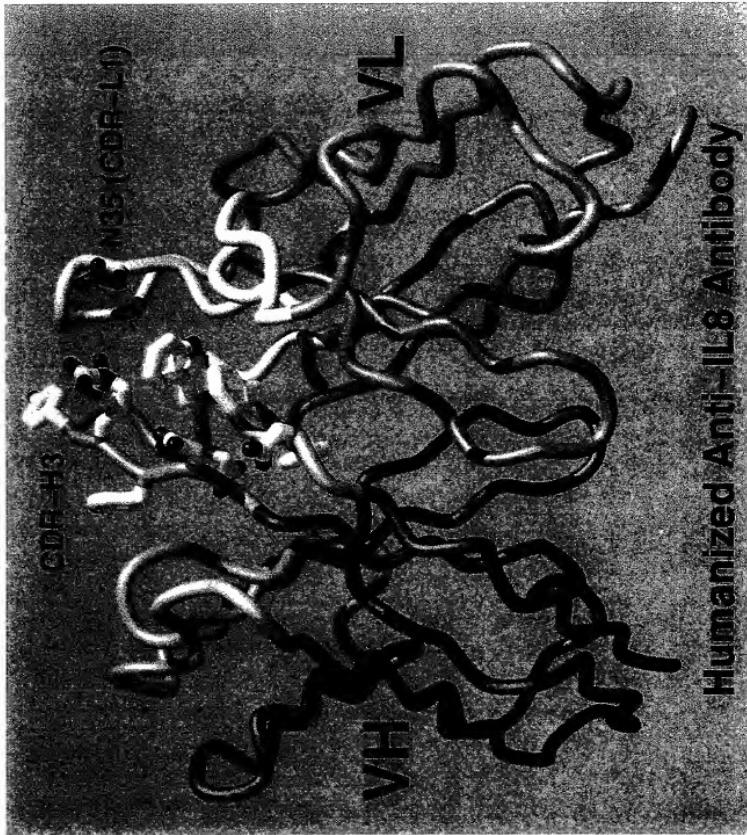
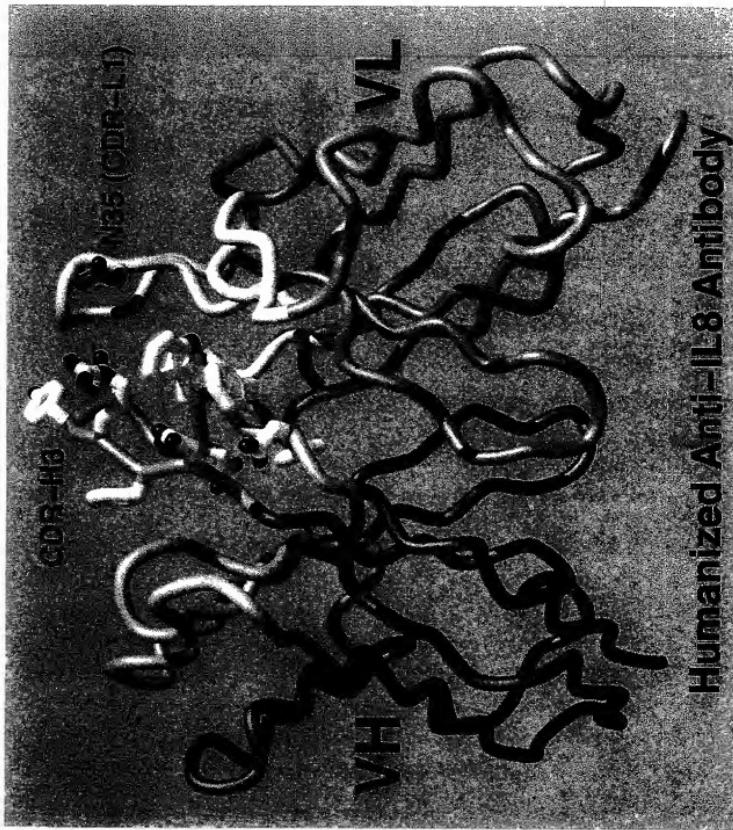


FIG. 32

Humanized Anti-IL8 Antibody



Y04560-B5292Z53



Humanized Anti-IL8 Antibody
FIG. 32

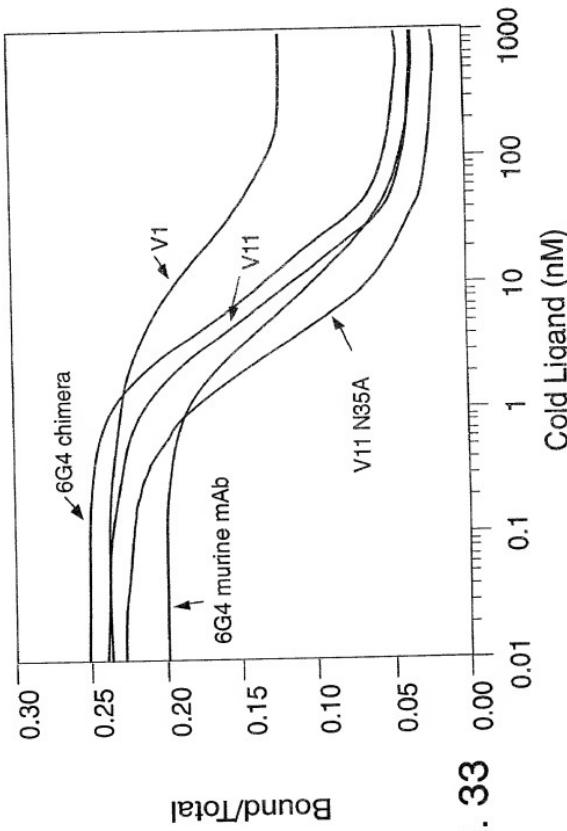


FIG. 33

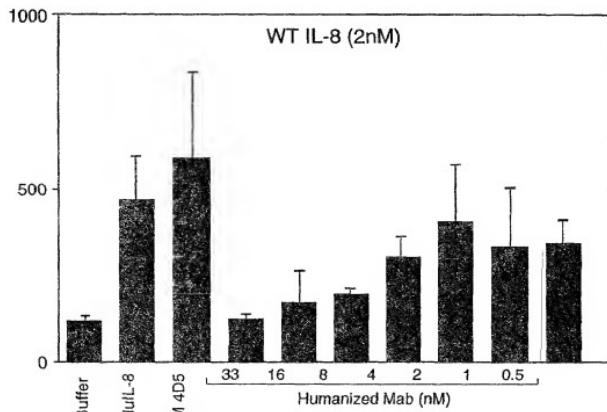


FIG. 34A

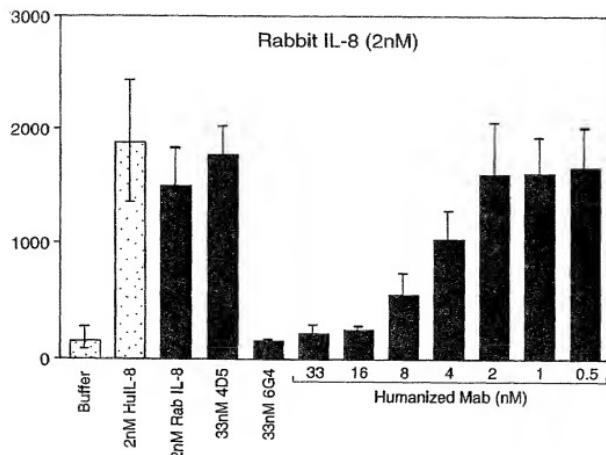


FIG. 34B

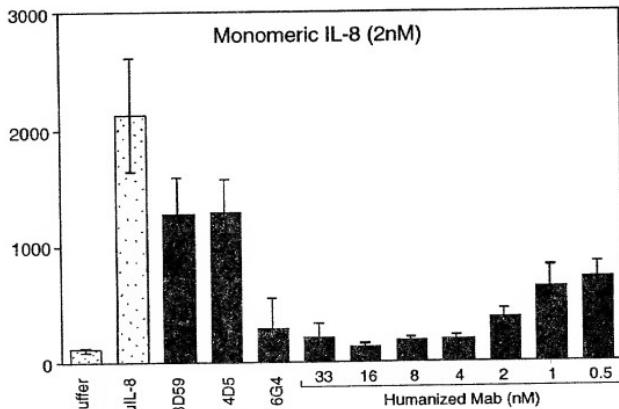


FIG. 34C

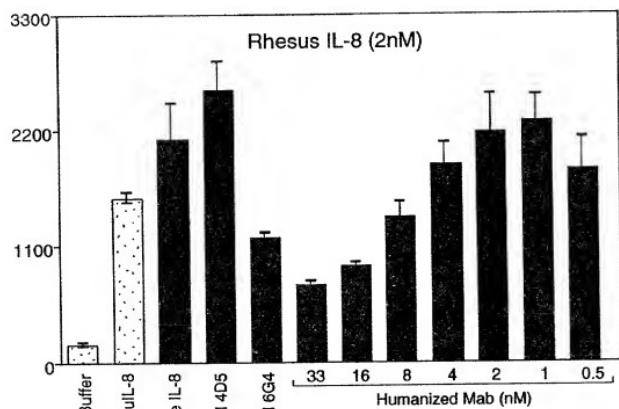


FIG. 34D

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V1N35A Light Chain

MKKNIAFLLASM**E**FSIATNAAYADIQMTQS**P**SSLASAVGDRY**T**ITCRSSQSLVH**G**ATY
LHWYQQKPGKAPKLLIYKVSNRFSGVP**S**RFS**G**SG**G**TD**F**TLT**I**SS**L**Q**O**PEDFATYYC**S**QT
HVLPLTFGGT**K**VEIKRTVAAPS**V**FIFPSD**E**QL**K**SG**T**ASV**C**ILLNFYPREAK**V**QW**K**VDN
ALQSGNSQ**E**ST**V**TEQ**D**SK**K**DT**S**TY**T**LS**S**ST**L**TL**S**KADYE**H**KV**Y**ACE**V**TH**Q**GL**S**SP**V**T**K**SFN**R**
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V1N35A Heavy Chain

MKKNIAFLLASM**E**FSIATNAAYEV**Q**LVOSGGGLV**O**FG**G**SLRLSCAA**S**GY**F**SSSH**Y**
W**R**Q**A**PG**K**GLE**M**GY**T**D**P**SG**N**GETTY**N**Q**K**FK**G**RFT**L**SRDN**S**KNT**A**YL**Q**M**N**SLRAED**T**AVYY
CARGDYRYNGDWFFFD**D**VG**G**GT**L**TV**V**SS**A**ST**K**GP**S**VF**P**LA**P**SS**K**ST**S**GG**T**AA**L**GCL**V**KD**Y**
P**E**P**V**T**V**SW**N**SG**A**LT**G**Y**T**FP**A**VL**Q**SS**G**LY**S**SS**V**T**V**P**S**SS**S**LG**T**Q**T**Y**T**TC**N**W**N**HK**P**S**N**TK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELGGRMKQLEDKVELLSKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35

1 ATGAAAAAAGA ATATCGCATTC TCTTCTTGCA TCTATGTTGC TTTTTTCTAT TGCTACAAAC
 TACTTTTCT TATAAGCGTAA AGAAGAACGT AGATACAAAC AAAAAGATA ACAGATGTTTG
 -23 M K K N I A F L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CGCAGCTCCC TGTCGGCCTC TGTCGGCGAT
 CGTATGGCAC TATAGGTCTA CTGGGTCAAGG GGCTCGAGGG ACAGGGCGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCGAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
 TCCCACTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACAGATGCATA
 18 R V T I T C R S S O S L V H G I G A T Y

181 TTACACTGGT ATCACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTAA CAAAGTATCC
 AATGTGACCA TAGTTGCTT TGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

241 ATTCGATTCT CTGGAGTCCTC TTCTCGCTTC TCTGGATCGC GTTCTGGGAC GGATTTCT
 TTACCTAAGA GACCTCAGGG AAAGAGCAAG AGACAGCTTCA CGAACACCTG CCTAAAGTCA
 58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCACATCA GCAGTCTGCA GCCAGAAAGAC TTGCAACTT ATTACTGTT ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGCTCTCTG AAAGCTGAA TAATGACAAG TGTCATG
 78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCGCCG TCACGTTGG ACAGGTGACG AAGGTGGAGA TCAAACGAAC TGTCGGCTCA
 GTACAGGGCG AGTCAAAACC TGTCCTATGG TTCCACCTCTG AGTTTGCCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGAAAC TGCTCTGTT
 GGAGACAGA AGTAGAACGG CGGTAGACTA CTGCTCAACT TTAGACCTTG ACAGAACGAA
 118 P S V F I F P P S D E C L K S G T A S V

481 GTGTGCTCTGC TGAATAACATT CTATCCCAGA GAGGCAAG TACAGTGAA GTGTGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGGTTA GCCCCATTGAG GTCTCTCTCA CAGTGTCTCG TCCTGTCTGG CCTGTCCTGG
 158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACAGAACACA CAAAGTCTAC
 ATGTCGGAGT CGTCCTGGGA CTGGGACTCG TTCTGTCTGA TGCTCTTGT GTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCTGAGC TCGCCCGTCA CAAAGAGCTT CAAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCAGGGCAGT GTTCTCGAA GTGTCTCCCT
 198 A C E V T H Q G L S S P V T K S F N R G
 (SEQ ID NO.58)

721 GAGTGTAAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTCAAAATTC GACTAGGGAGA TGCGGCCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
 218 E C O (SEQ ID NO.56)

FIG. 36

DRAFT

781 AAAAGGGTAT CTAGAGGTG AGGTGATTT ATGAAAAAGA ATATGCATT TCTTCCTGCA
 TTTTCCATA GATCTCCAAAC TCCACTAAAA TACTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A

841 TCTATGTTCG TTTTTCTAT TGCTACAAAC CGGTACGCTG AGGTTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGA TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CGCCCACCG ACCACGTCGG TCCCCGAGT GAGGCAAACA GGACACGCTG AAAGCCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y

961 TCTCTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGTATCGTGGACCCAG CGACTGGGG GCCCATTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGA ACTACGTATA ATCAAAGTT CAAGGGCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCAAT TAGTTTCAA GTTCCCGCA
 48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTGGCGACAA CTCCAAAAC ACAGCATACC TGCAAGATGAA CAGCCTGCGT
 AAGTGAATA GGCGCTGTTG AGGTGTTTG TTGCTGTATGG ACGTCTACTT GTCGGACCGA
 68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGGCGCTCA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGAATGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGAGC TCTGGGGTCA AGGAACCCCTG GTCACCGCT CTCAGGCCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCGAT TCTCTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
 108 E F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCTCC AAAGAGCACCT CTGGGGGAC AGGGGCCCTG
 GTTAGGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCTGGA GACCCCGCTG TGGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L

1321 CGCTGGCTGG TCAAGGACTA CTTCCCGAAGG CCGGTGACGG TGTCTGGAA CTCAGGGGCC
 CGACGCCAGC AGTTCCTGTAGA GAAGGGGCTT GGCACACTGG ACAGCACCTT GAGTCGGCG
 148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAAGCG GGGTGCACAC CTTCCCGGCT GTCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTCGC CGCACGTG TGAGGGCCGA CAGGATGTC GAAGGTCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGC CTCCAGCAGC TTGGGACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTGCTG AACCCGTGGG TCTGGATGTA GACGTGCGAC
 188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTCG GGTGTTGTG GTTCCAGCTG TTCTTCAC TCGGGTTTAG AACACTGTCTT
 208 N H T P S N T K D K V K E P K S C D K

1561 ACTCACACAT GCGCCGGCTG CCCAGCAGCA GAACTGCTGG GGGCCGCAT GAAACAGCTA
 TGAGTGTGA CGGGCGGCAC GGGTCGTTGGT CTTGACGACC CGCCGGGTA CTTGTCGAT
 228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

201309-0592650

1621 GAGGACAAGG TCGAAGAGCT AACTCTCCAAG AACTACCACCC TAGAGAACATGA AGTGGCAAGA
CTCCTGTTC AGCTTCTCGA TGAGAGGTTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B

19750-3522460

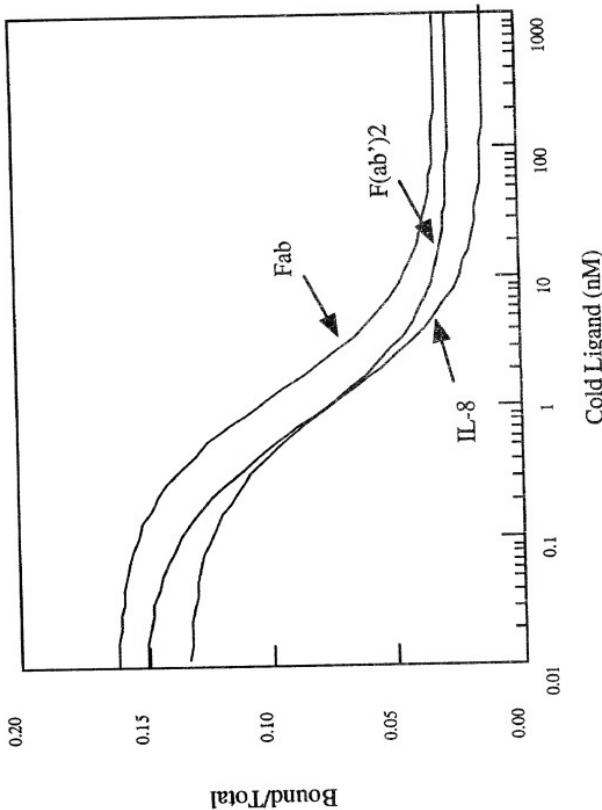
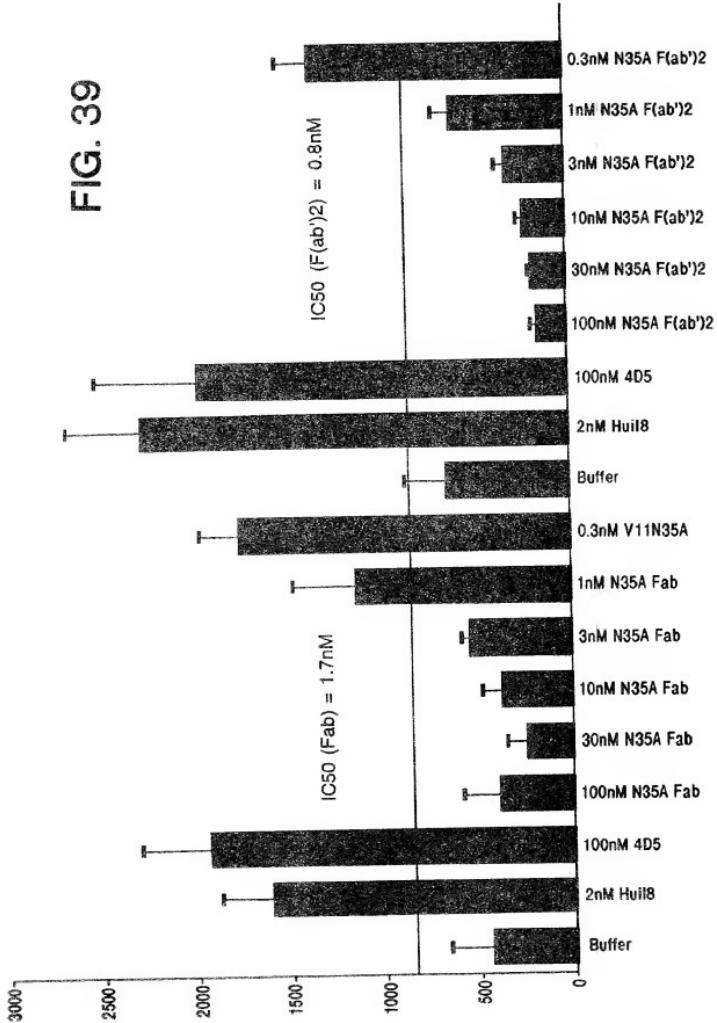


FIG. 38

FIG. 39



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FIG. 40

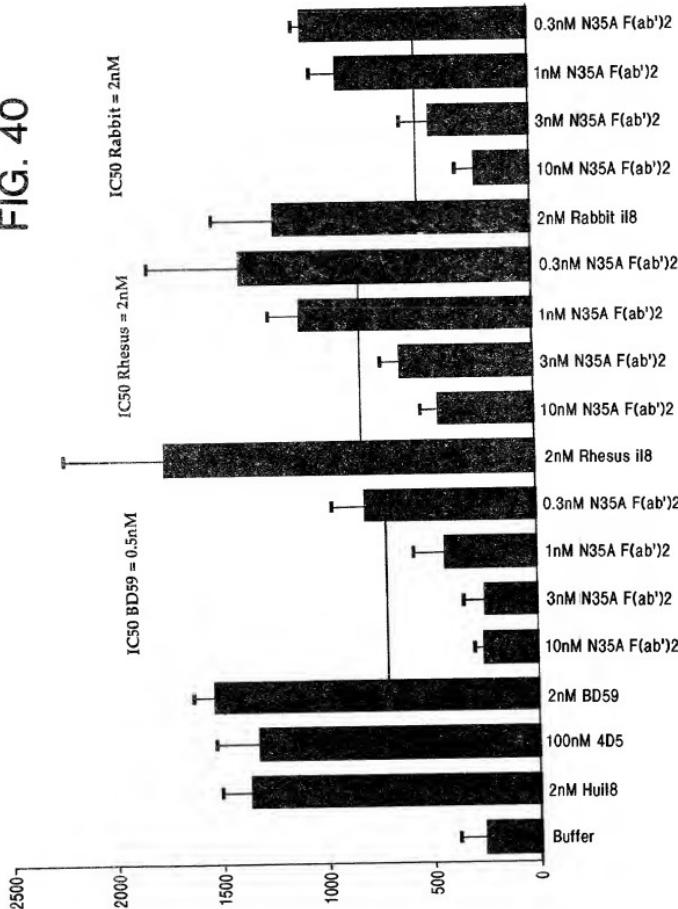


FIG. 41A

scrfI
 nclII
 msP I
 hpa II
 dsAV
 xmaI/pspAI
 smaI
 scrFI
 nclI
 dsAV
 cauII
 bsaII
 null
 avA I
 sau3AI tagI
 rsaI
 mbuI/ndeII [dam-]
 dpuI [dam]
 cep6I
 nlaIV
 nlaIV Paek7I
 kpnI cauII dpuI [dam-]
 hincI
 bsrF I/xbaII
 bani bsaII alwI [dam-]
 bamiII
 avA I
 alwI [dam-] mnlI
 acc65I
 TCGAACCCG GGGATCCCT CGAGGTGAG GTGATTGATTA GAAAGGAT ATTCGTCATC TTTCTCATG CTCAGACG
 AGCTATGGC CCCTTGAGA GCCTGAACTC CACTAACTA CTTTCTCA TAGCTGAAAG AAGCTGAG ATTACAGAA AAAGATTAAC GATTTGCG
 -23 a mutation was found that inactivated the mnlI site. The penultimate nucleotide was changed from G to T.
 sstI
 sacI
 hgIJI
 hgIAl/AspHI
 ecII136I
 bsp1286
 bsmFI bmyI
 bsrI avai aluI
 tthII/AspI banII
 ecory
 501 ATTCGCTAT ATTCGAGATA CCCAGTCGCC GAGTCGCCG TGGCCATAG TGCCGCTCG ACCGCAAGT CAAGTCAGG CCTAGTACAT
 TATCCACTA TAGCTCTCT GGCTGAGGGG CTAGGGAGAC AGGGAGAGC ACCGCTATC CGCTGCTAG TGGCTGCA GTTCGTCG GAAATGATTA
 -2 Y A D I Q M T Q S P S S L S A V G D R V T C R S S Q S L V H

FIG. 41B

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FIG. 41C

It is also important to note that the results of the study were not statistically significant.

FIG. 41D

FIG. 41E

-5 T N A Y A E V Q L V Q S G G L Y Q P G G S L R L S C A A S G Y S

1201 AGTCGAC TAGCTAA AGGGTATC AGAGGTGAG GTGATTAT GAAAGAT ATCCATTTC TTCTGATC TCATCGTT ATCAGATT TCCATAGA TCCCACTC CACTAACTA CTTGGTAAG AAGAGCTG ATACAGCAA M K K N I A F L L A S M F V F S I A	rsal mael bfaI speI ecspI	mael mael bfaI mael bfaI	hpII xbal mluI mluI mluI	mbolI sfANI mbolI sfANI	
-23 rsal bsWI/SphI thaI fndII/mvaI	bsWI bsWI bsWI bsWI bsWI	mael mael mael mael mael	mael mael mael mael mael	hpII xbal mluI mluI mluI	hpII xbal mluI mluI mluI
1301 CTACAAACC GTACGTGAG GTTCAGCTAG TCCAGTGAG CGGTGACTC CGGTGACCT CGGTGACCT GATCTTGC CAGCACTC CAAGCTGTC AGCTAGAC GCACCTGGAC GCGAAACGG AGACCTGGA GACGGTAG -5 T N A Y A E V Q L V Q S G G L Y Q P G G S L R L S C A A S G Y S	scrFI scrFI scrFI scrFI scrFI	scrFI scrFI scrFI scrFI scrFI	mvaI ecoriI dsav mvaI ecoriI	mvaI ecoriI dsav mvaI ecoriI	fru4HI ecoriI dsav fru4HI ecoriI
					aluI aluI [dcm-] fru4HI bsrI
					bbvI bbvI
					bsrI bbvI

FIG. 41F

FIG. 41G

FIG. 41H

FIG. 411

FIG. 41J

FIG. 41K

FIG. 41L

bsrI	CGGGGTGCC TTACTGTTA GCAGATTA	bsrI	TGCTTCGCA GACATGAGC TGTGACTGT
bsrII	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT	bsrII	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
bsrIII	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT	bsrIII	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
bsrIV	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT	bsrIV	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
bsrV	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT	bsrV	TTTCTTCTTCTTCTTCTTCTTCTTCTTCTT

FIG. 41M

FIG. 41N

FIG. 410

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FIG. 41P

FIG. 41Q

tru9I	nlaIV hgtCI bamI	sau3A1 mbpI/ndeII[dam-] donII[dam+]	phiE hinfI	maiI
mesI	mnII	ddeI	fokI	akdI/mael05I
33501	CCGATGCTTA ATGAGTGG GCGAACATC TACGACCT	CACCTTCG ACCGTTCTT TGCTCATGCT GTGGATGAG	TCCCTGCTT AGTCAATAG GAGGACATA AGGAGCTAG	GATACGGAG CTATGGCTC

FIG. 41R

FIG. 41S

FIG. 41T

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FIG. 41U

>length: 6563

1645 6489
aaII(GCCTC): 403 823
acc651(GCINCC): 1093 1563 4449
aci(CTTAC):
acII(CCGGA): 3867(dam-1)
178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2946 3094 3141 3226 3341 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4471 4505 4518 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
see hinII
acVI
afII(ACRGT):
age(ACCGT): 1788
ahaiI/BashII(GRCGC): 1645 1813 2616 2637 2751 3408 6107 6489
ahaiII/drai(CTTAA): 5435 5434 6146
ahaiII/drai(CTTAA): 346 5566
ahII/eamII/6SI(GACNNNNNGTC): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2246
2218 2233 2899 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
alII(AcII):
alw44I/snoII(GRGCAC): 5922
alwII(dam-1)(GATTC): 1831 4494 4992 6238
alwII(dam-1)(GATTC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
alwII(dam-1)(GATTC): 6196 6214
alwII(dam-1)(GATTC): 1117 1385 5089
apaI(GGCC): 1695
apaII/ENDI(GTGCA): 1831 4494 4992 6238
apoII(RATTI): 1 331 4033
apoII(dam-1)(CTGGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333
aseI/aseII/vspI(ATTAAT): 5742
aseII: see aseI
aniI: 905 930 4234 6166
asp700(GAANNNNNTC): 403 823
asp718(GGTACCC): 403 823
aspH: see hgtAI
aspI: see tthIII
aspI: 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
asuI(GNCAC):

FIG. 4.1V

Y OTTSESO "ES2932260

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42

Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

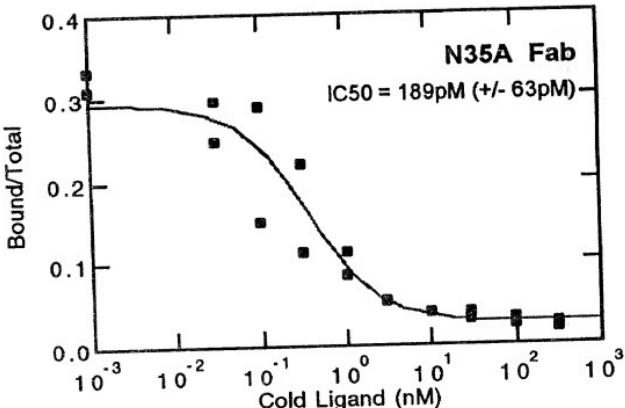


FIG. 43B

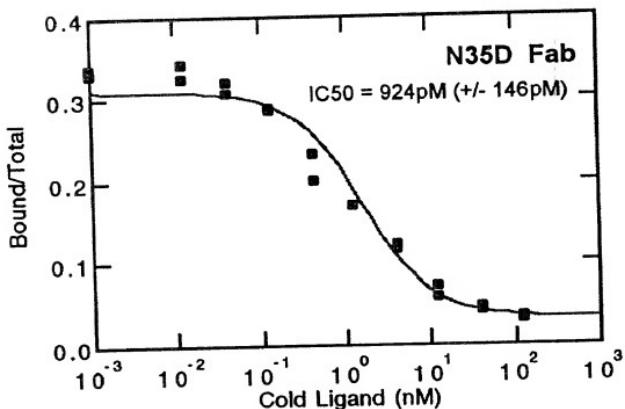


FIG. 43C

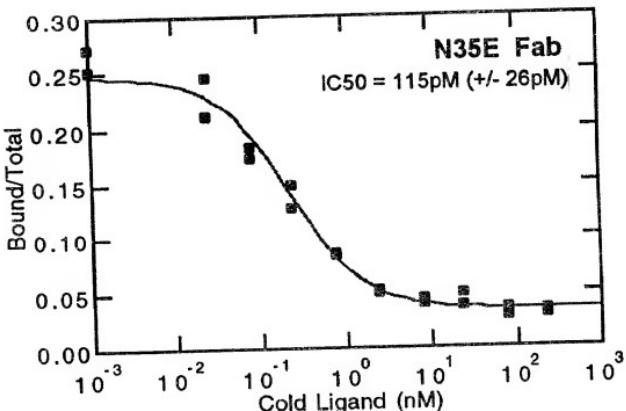


FIG. 43D

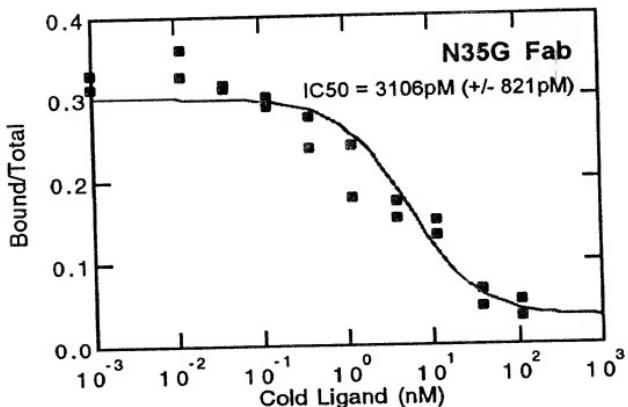
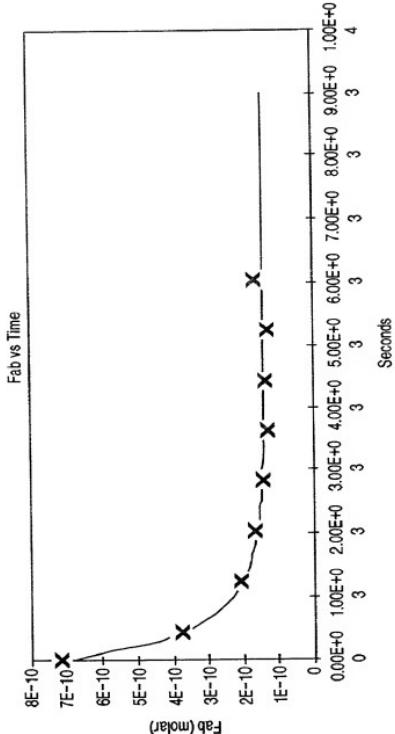


FIG. 43E

7/17/2010 9:53:52 AM



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂

SAMPLE	k_a	k_d	K_d
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0×10^6	2.1×10^4	109pM
6G4V11N35E-Fab	4.7×10^6	2.6×10^4	54pM

FIG. 4.4

1 ATGAAAAAAGA ATATCGCAIT TCTTCTTGCA TCTATGTTCG TTTTTCTAT TGCTACAAAC
 TACTTTTCT TATAGCTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTG
 -23 M K K N I A F L L A S M F V F S I A T N

61 GCAATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCGGCCTC TGTTGGCGAT
 CGTATGGCAC TATAGGTCTA CTGGGTCAAGG GCCTCGAGGG ACAGGCCGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
 TCCCAAGTGT AGTGAGGTC CACTTCAGTT CGAATCATG TACCATATTC ACTCTGCATA
 18 R V T I T C R S S O S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGTCCT TGTCCTTTT CGAGGCTTTC ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTCTACT
 TTACCTAAGA GACCTCAGGG AAAGCCGAAAG ACAGCTAGGC CAAGACCTTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCACATCA GCAGTCGCA GCCAGAACAC TTTCGCAACTT ATTACTGTTT ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGTCTCTG AAGCGTTGAA TAATGACAAG TGTCATGAA
 78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCGGC TCACGTTGAC AAGGGTACCA AGGTTGAGA TCAAACGAC TGTCGCTGCA
 GTACAGGGACG AGTCAAAACCG TGTCCATGG TTCCACCTTG AGTTTGCTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTGA AATCTGGAAC TGCTCTGTT
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTCGCTGC TTGATAACCTT CTATCCCGAGA GAGGCCAAAG TACAGTGGAA GTGTTGATAAC
 ACAGCGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTAA GCCCATTGAG GGTCTCTCA CAGTGTCTG CCTCTCGTT CCTCTCGTGG
 158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCCT GAGCCTGAGC AAAGCAGACT ACAGGAAACAA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCGA TGCTCTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCTGCGAAG TCACCCATCA GGGCTGAGC TCGCCCGTCA CAAAGAGCTT CAAACAGGGAA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCGAA GTTTCGCCCT
 198 A C E V T H Q G L S S P V T K S F N R G

(SEQ ID NO.65)

721 GAGGTGTTAAG CTGATCTCTC ACAGCCGGAGC CATCGTGGCC CTAGTACCCCA ACTAGTCGTA
 CTACAAATTC GACTAGGAGA TGCGGCTTCG CTAGCACCGG GATCATGGT TGATCAGCAT
 218 E C O (SEQ ID NO.62)

FIG. 45

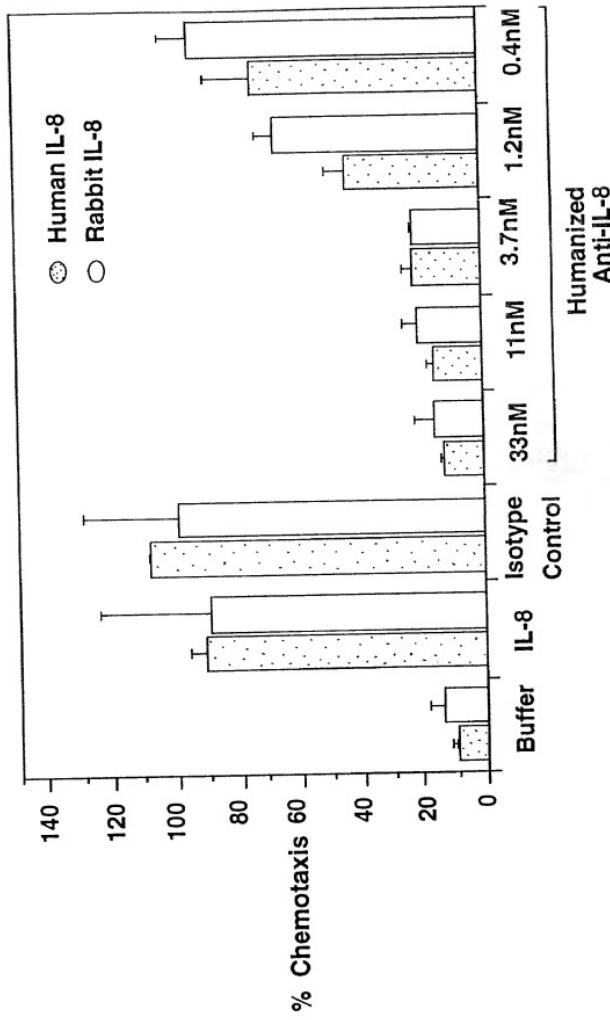


FIG. 46

FIG. 47

Bold indicates nucleotide change destroying PvuII site.

N35AH1^{upr}
5'-CTAGTGCAGTCAGGGCTGGTGCAGGGGCTCACTCCGTTGTGCAGCTCTGGCTACTCCTTC-3'
(SEQ ID NO.6)

N35AH1^{lwr}
5'-TCGAGAAGGAGTAGCCAGAACGGACAAACGGAGTGA
AG-3'

N35AH1^{upr}
5'-CTAGTGCAGTCAGGGCTGGTGCAGGGGCTCACTCCGTTGTGCAGCTCTGGCTACTCCTTC-3'
(SEQ ID NO.6)

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FIG. 48B

FIG. 48C

601 CAAGATGA CCACACCC TCTGTTGGAA GGTAAACAGA ATTCACCTT CCACTGCCT TAGACACTTA ATACCATCC TTGACACCA
 GTTCTTACCT GGTTGGAG AACATCCTT CCACTGCCT TAGACACTTA ATACCATCC TTGACACCA

601 CAAGATGA CCACACCC TCTGTTGGAA GGTAAACAGA ATTCACCTT CCACTGCCT TAGACACTTA ATACCATCC TTGACACCA
 GTTCTTACCT GGTTGGAG AACATCCTT CCACTGCCT TAGACACTTA ATACCATCC TTGACACCA

scrFI
 mvaI
 msel
 tflI
 hinfI hphI
 alwII [dem+]
 ec1136I
 bsp1286
 baiHKA I
 bpuI
 hgiII / AspHI
 ec1136I
 bsp1286
 baiHKA I
 bpuI
 mnlI aluI
 bseI banII
 bclI bearI
 accI acacI / AspI
 truGI
 msel
 aseI / asciI / AspI
 701 AGGAGAGAT TAAATAGTT CTAGTAGAG AACACACAGA ACCACACAGA AACACACAGA ACCACACAGA
 TCTGTCATA ATTATATCA GAGTCATTC TGGTTCTC TGGTGGCT

scrFI
 mvaI
 msel
 tflI
 hinfI hphI
 alwII [dem+]
 ec1136I
 bsp1286
 baiHKA I
 bpuI
 mnlI aluI
 accI acacI / AspI
 bsaI
 801 AGAACCGAA TGGGAGAT AGTGGAGAT GGTGGAGCA GTTGTGTTA CGTGTGTTA CGGACACCT TACGCTCTT
 TGTGCTCTT AACCTCTAT TCACTCTA CCAACCTAT CAACTCTAT CAACTCTAT CAACTCTAT CAACTCTAT

scrFI
 mvaI
 msel
 tflI
 hinfI hphI
 alwII [dem+]
 ec1136I
 bsp1286
 baiHKA I
 bpuI
 mnlI aluI
 accI acacI / AspI
 bsaI
 801 AGAACCGAA TGGGAGAT AGTGGAGAT GGTGGAGCA GTTGTGTTA CGTGTGTTA CGGACACCT TACGCTCTT
 TGTGCTCTT AACCTCTAT TCACTCTA CCAACCTAT CAACTCTAT CAACTCTAT CAACTCTAT CAACTCTAT CAACTCTAT

scrFI
 mvaI
 msel
 tflI
 hinfI hphI
 alwII [dem+]
 ec1136I
 bsp1286
 baiHKA I
 bpuI
 mnlI aluI
 accI acacI / AspI
 bsaI
 801 AGAACCGAA TGGGAGAT AGTGGAGAT GGTGGAGCA GTTGTGTTA CGTGTGTTA CGGACACCT TACGCTCTT
 TGTGCTCTT AACCTCTAT TCACTCTA CCAACCTAT CAACTCTAT CAACTCTAT CAACTCTAT CAACTCTAT CAACTCTAT

hgII
 hinII/acyI
 ahaiI/bshII
 sorFI
 mvaI
 mnII
 dsaV
 ecorII
 dsbNI
 asyI(dam+)
 bsaII
 ddel
 GTCGTCCTG
 CAGGAGAC

 nlaIII
 mbpI/ndeII [dam-]
 dprI/dam+]
 dpuII [dam-]
 maellI alwI [dam-]
 apoI
 afiliI
 maellI
 901 GRACAGAGA TGATCAGGA ATTGTGGT
 GRACAGTG TGATCAGGA ATTGTGGT
 TCCGAAAT TGATTGGG AAATATAAC CTCCTCCAGA ATACCAAGC
 AGGCTTA ACTAACCC TTATGATTC GAGAGGCT TATGATTCG
 CTGCTCT ACTAGTCCT TAACCTCA CTGTCGAAAA

 sorFI
 mvaI
 ecorII
 dsaV
 betNI
 asyI (dam+)

 sat96I
 avall
 9001 AGCGCAGGA GAAahAGGC ATCAGTATA AGTTGAACT
 TCCGATCC CGTTTCG TACTCATCA GATGACTCA

 sfaNI
 mnII
 accl
 mbolI
 ftsI
 9001 AGCGCAGGA GAAahAGGC ATCAGTATA AGTTGAACT
 TCCGATCC CGTTTCG TACTCATCA GATGACTCA

 styI
 bsaII

 nlaIII
 mbpI/ndeII [dam-]
 dprI/dam+]
 dpuII [dam-]
 bshII
 betNI
 cec8I
 betNI
 dsaV
 bsmPI
 naiI
 Ppu10I
 naiI/AvalII
 mpaII
 1101 AGCGTATT ATTAACAT CGGAACT
 TCCGAAAT TATTCGTA GACCGAAC
 GAACTGAC GAACTGAC

 sfaNI
 mnII
 accl
 mbolI
 ftsI
 1101 AGCGTATT ATTAACAT CGGAACT
 TCCGAAAT TATTCGTA GACCGAAC
 GAACTGAC GAACTGAC

 styI
 bsaII

 sat3AI
 mbpI/ndeII [dam-]
 dprI/dam+]
 dpuII [dam-]
 bshII
 betNI
 cec8I
 betNI
 dsaV
 bsmPI
 naiI
 Ppu10I
 naiI/AvalII
 mpaII
 1101 AGCGTATT ATTAACAT CGGAACT
 TCCGAAAT TATTCGTA GACCGAAC
 GAACTGAC GAACTGAC

FIG. 48D

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FIG 48E

FIG. 48F

FIG. 48G

FIG. 48H

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FIG. 48I

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FIG. 48J

3001 GATTTGCT CAGTTAGGT GTGGAAAGTC CGCAAGTC CCAGCAGGC GGTGCGGAG GGTGTCCTC CTTCATAGT TTGCTAGTA
 CTTACGACA GTCRATCCCA CTCCTTCAG GGTGCGGAG GGTGTCCTC GGTGCGGAG GGTGTCCTC
 H1/H1V
 serPFI
 mvaI
 ecorII
 ddeV
 bsrNI
 apyII(dcm+)
 bsaDI
 bsaFI
 bsaMI
 bsaFI
 3101 GATTTGCT CAGTTAGGT GTGGAAAGTC CGCAAGTC CCAGCAGGC GGTGCGGAG GGTGTCCTC CTTCATAGT TTGCTAGTA
 CTTACGACA GTCRATCCCA CTCCTTCAG GGTGCGGAG GGTGTCCTC GGTGCGGAG GGTGTCCTC GGTGCGGAG GGTGTCCTC
 H1/H1V
 serPFI
 mvaI
 ecorII
 ddeV
 bsrNI
 apyII(dcm+)
 bsaDI
 bsaFI
 bsaMI
 bsaFI
 3101 TCCTCAGCT CCCAGCAGG CAGAAGTAGT CAGAGCAGTC ATCTGATTA CTCGAGAACC AGATGCGGCC CCGCTACTTC
 GGGGTCGGA GGGTGTCCTC GTCTTCATAC GTTCTCTAG TAGATTTAT CAGTCGTTG TTTCTGGGG GGTGATGGG CGGTGATGGC
 AGGGGTCGGA GGGTGTCCTC GTCTTCATAC GTTCTCTAG TAGATTTAT CAGTCGTTG TTTCTGGGG GGTGATGGG CGGTGATGGC
 H1/H1V
 serPFI
 mvaI
 ecorII
 ddeV
 bsrNI
 apyII(dcm+)
 bsaDI
 bsaFI
 bsaMI
 bsaFI
 3201 GCGCCAGTC CGCCCATTCG CGGCCGCTG GGTGCGGAG GGTGTCCTC AATGCTTCG AACGCTTAA
 GCGGGTCTAG GCGGGTCTAG GCGGGTCTAG GCGGGTCTAG

FIG. 48K

FIG. 48L

FIG. 48M

FIG. 48N

FIG. 480

FIG. 48Q

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FIG. 48S

FIG. 48T

FIG. 48U

FIG. 48V

FIG. 48W

FIG. 48X

FIG. 48Y

tr91
 msel
 ase1/asnl/vspl
 xnnl
 8101 nlaIII asp700
 8101 TGACCATAT TACGATTAA (SEQ ID NO.68)
 ATCTGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC): 1690 5947
 acg551(GGTACCC): 2995 3967 4529
 acG1(STMKAC): 823 1039 2738 4237
 acII(CCCTC): 217 238 250 260
 acII(CCCTC): 3167 3119 3188 3200 3220 3221 3267 3404 3449 3686 3949 4021 4318 4512 4777
 acII(CCCTC): 4739 4748 4760 4770 4781 4827 4914 5070 5127 5153 5166 5203 5217 5220 5248
 5275 5680 5689 5741 5751 5790 5979 6026 6126 6334 6311 6355 6476 6522 6713 6804
 7156 7195 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070

see hanII
 786

acvI/bfri(CITRAAG):
 932 7758

aflII(ACRGT): 1833
 agel(ACCCGP): 968 1590 1658 5117 5947 6329
 ahaiII/bsai(BGCCGC): 696 4935 6390 6382 7001
 shaiII/draI(FTRRAA): 696 6665
 shdi/eam1105I(GACNNNNNTC): 2087
 5 44 336 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
 aluI(ACTT): 3562 3566 3676 3733 3732 4220 4268 4331 4344 4554 4842 4896 4954 5047 5333 5590
 5803 5822 6316 6519 6679 7200 7457 7533 7819 7937 8096

alw44I/anoI(GTGCGAC): 1876 5651 6198 7444

FIG. 48Z

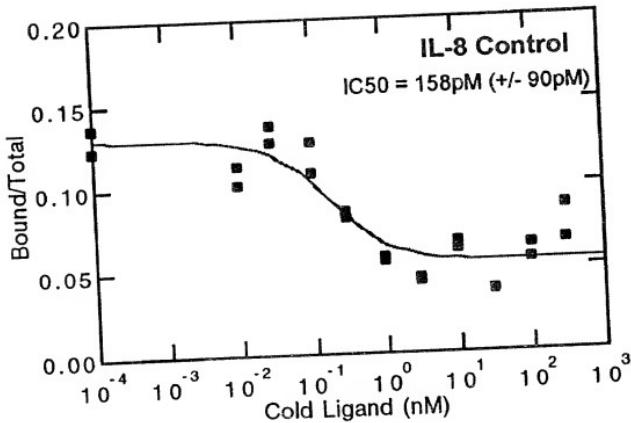


FIG. 49A

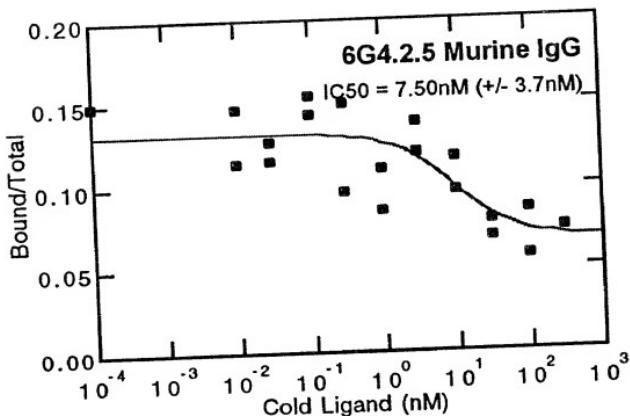


FIG. 49B

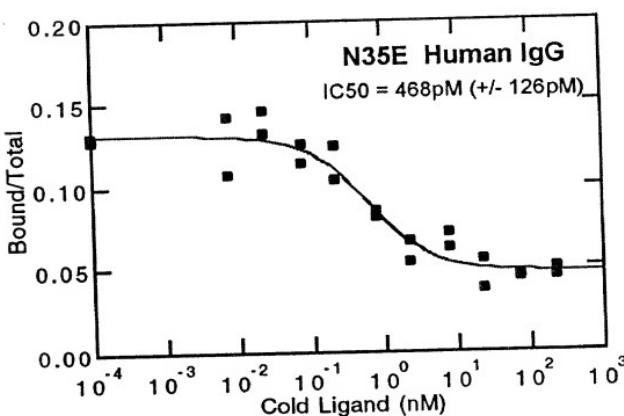
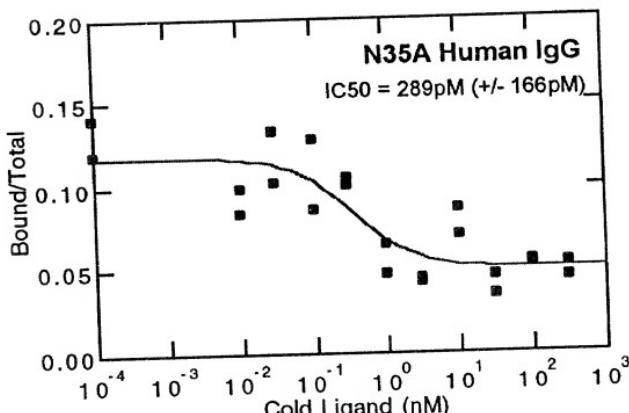


FIG. 50A

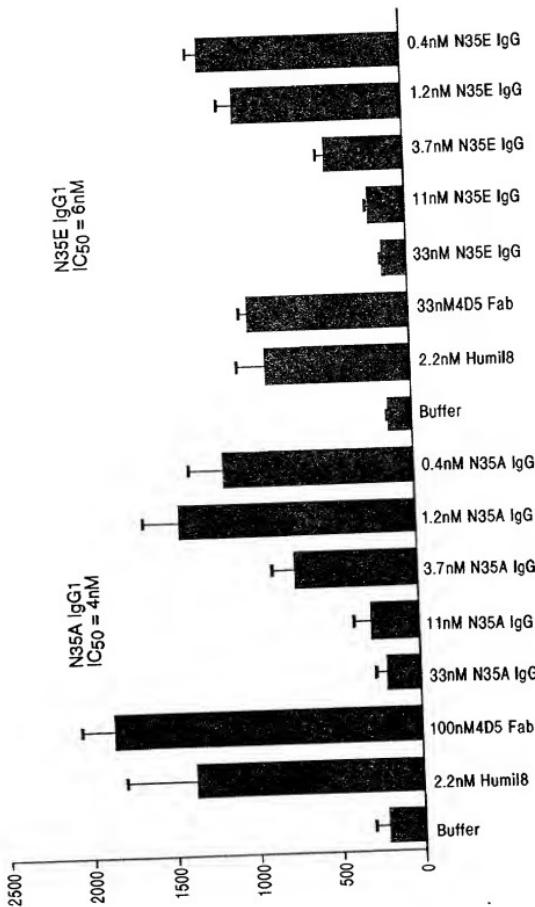
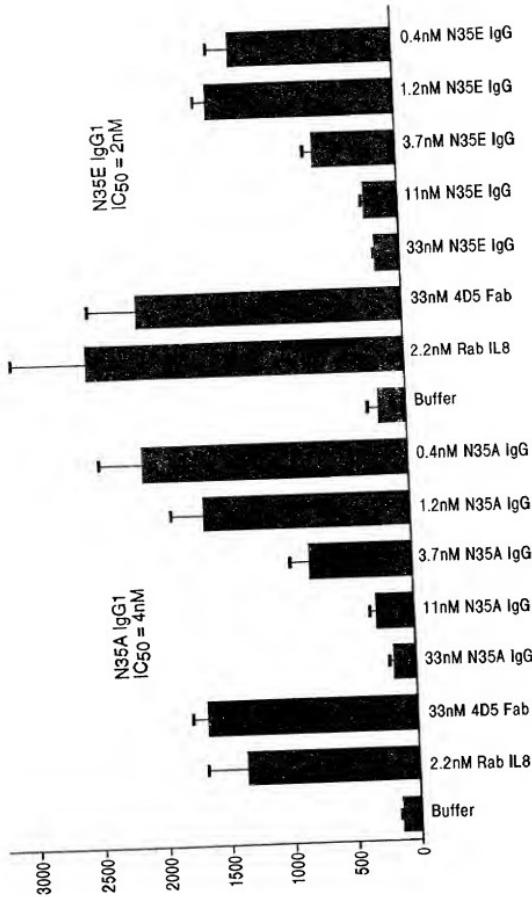
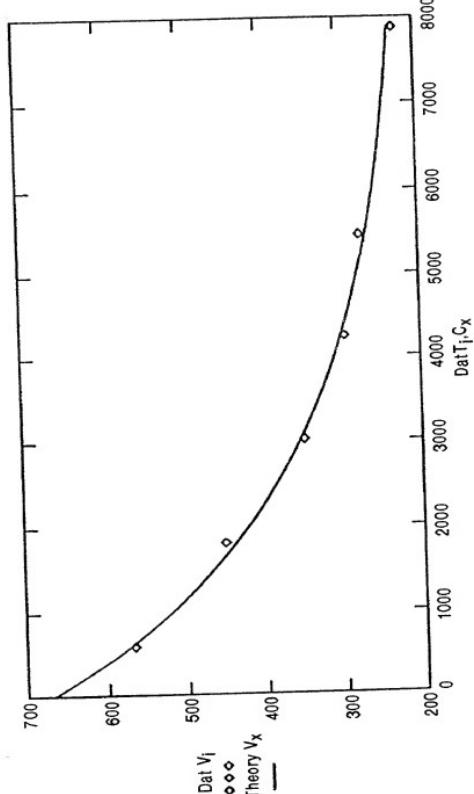


FIG. 50B





Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	k_a	k_d	K_d
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350 pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88 pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49 pM

FIG. 51

YOTE50-25292260

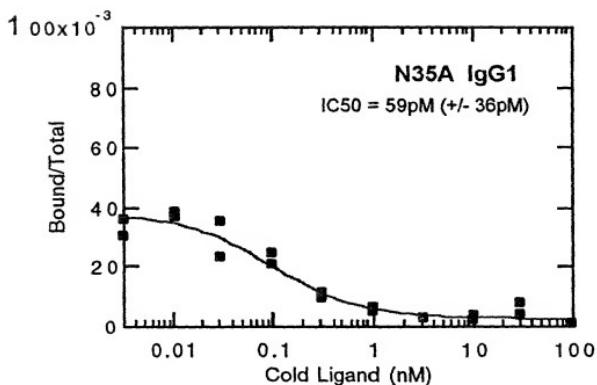


FIG. 52A

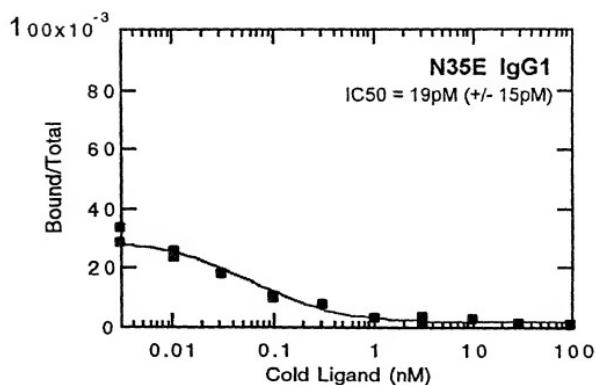


FIG. 52B

781 AAAAGGGTAT CTAGAGGTG AGGTGATTT ATGAAAAAGA ATATCGCATT TCTTCCTGCA
 TTTCCCAT A GATCTCCAC T C C A C T A A A A T C T T T T C T T A T A G C G T A A G A A G A A C G T
 -1 M K K N I A F L L A

 841 TCTATGTTCG TTTTTCTAT TGCTACAAAC GCGTAGCTG AGGTCAGCT AGTGCAGTCT
 AGATACAACC AAAAAGATA ACATGTTTG CGCATGGAC TCCAAGTCGA TCACGTCAGA
 -11 S M P V F S I A T N A Y A E V Q L V Q S

 901 GCGGGTGGCC TGGTCCAGCC AGGGGCTCA CTCCGTTMGT CCTGTGCAGC TTCTGGCTAC
 CGGCCACCG ACCACGTCGG TCCCCGAGT GAGGGAAACA GGACACCTCG AAAGACGATG
 8 G G L V Q P G G S L R L S C A A S G Y

 961 TCCCTCTCGA GTCACTATAT GCACTGGTC CGTCAGGCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGTATATA CGTGACCCAG GCAGTCGGG GCCCATTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

 1021 GTTGGATATA TTGATCCCTT CAATGGTAA ACTACGTATA ATCAAAGGTT CAAGGGCCGT
 CAACCTATTA AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTCAA GTTCCCGCA
 48 V G Y I D P S N G E T T Y N O K F K G R

 1081 TTCACCTPAT CTCCGCAACAA CTCCAAAAC ACAGCATACC TGCAAGATGAA CAGCTGGCT
 AAGTGAATA GAGGCTGTG GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTGCGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R

 1141 GCTGAGGACA CTGGCGCTTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGA
 CGACTCTGT GACGGCAGAT ATAGCACAGT TCTCTCTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

 1201 TTCTTCGAGG TCTGGGGTCA AGGAACCTG GTCACCGCTCT CCTCGGCCCTC CACCAAGGGC
 AAGAACGTCG AGACCCCACT TCCTTGGAC CAGTGGCAGA GGAGCCGGAG GTGGTCCCG
 108 F F D V W G Q G T L V T V S S A S T K G

 1261 CCATCGGTCT TCCCCCTGGC ACCCTCCCTCC AAGGACACTT CTGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGAGGAGG TTCTCGTGA GACCCCGGTG TGCGCGGAC
 128 P S V F P L A P S S K S T S G G T A A L

 1321 GGCTGCCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCC
 CCGACGGACC AGTCTCTGTAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCGGCG
 148 G C L V K D Y F P E P V T V S W N S G A

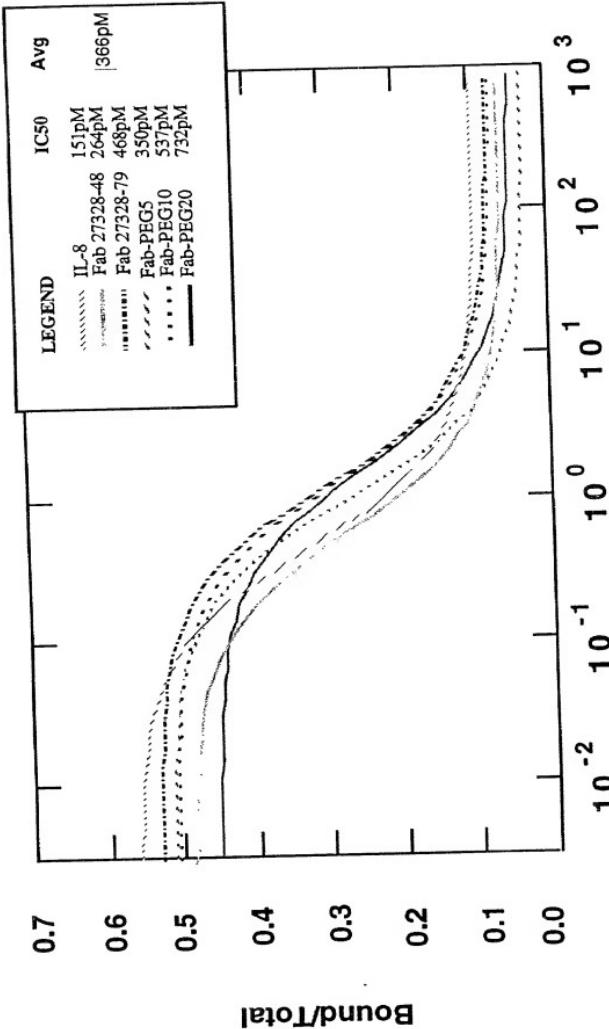
 1381 CTGACCGAGG CGCTGCCACAC CTTCCCGGCT GTCTCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTCGC CGCACGTGTA GAAGGGCCTA CAGGTCTCA GGAGTCTGTA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

 1441 AGCACCGTTCG TGACCGTGC CTCAGCAGC TTGGGCCACCC AGACCTACAT CTGCAACGTG
 TCGTCGACCC ACTGGCACCG GAGTCGTCG AACCCGIGGG TCTGGATGTA GACGTGAC
 188 S S V V T V P S S S L G T Q T Y I C N V

 1501 AATCACAAAG CCAGCAACAC CAAGGTCGAC AAGAAAGTT AGCCCAATC TTGTGACAAA
 TTAGTGTTCG GGTCTCTGTG GTTCCAGCTG TTCTCTCAAC TCGGGTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K

 1561 ACTCACACAT CCCGCCGTGA (SEQ ID NO.69)
 TGAGTGTGTA CGGGGGCACT
 228 T H T C P P O (SEQ ID NO.70)

FIG. 54A



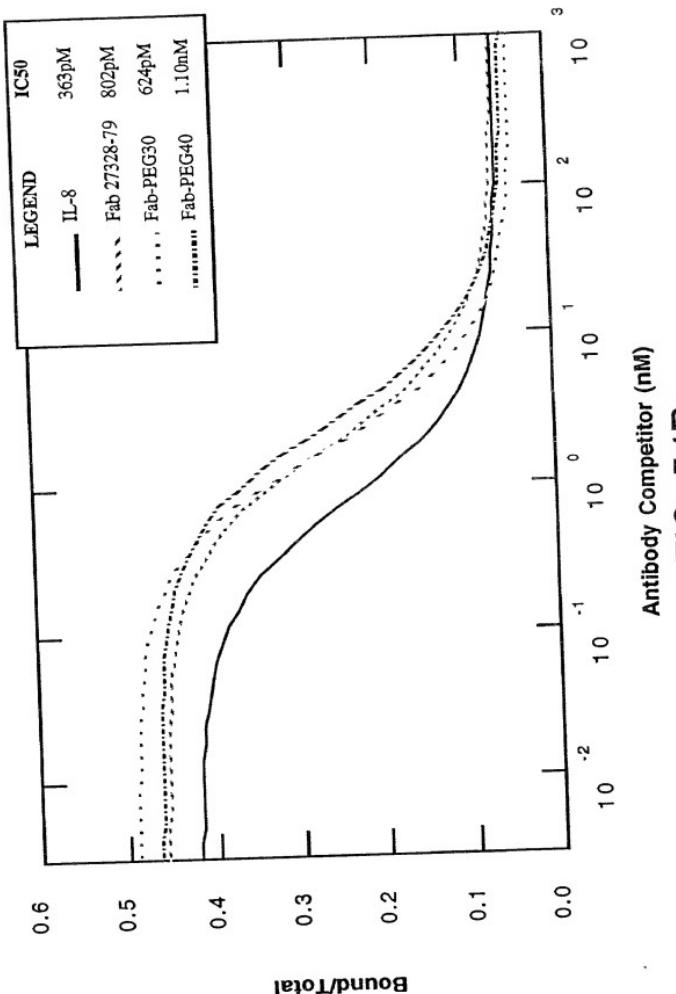


FIG. 54B

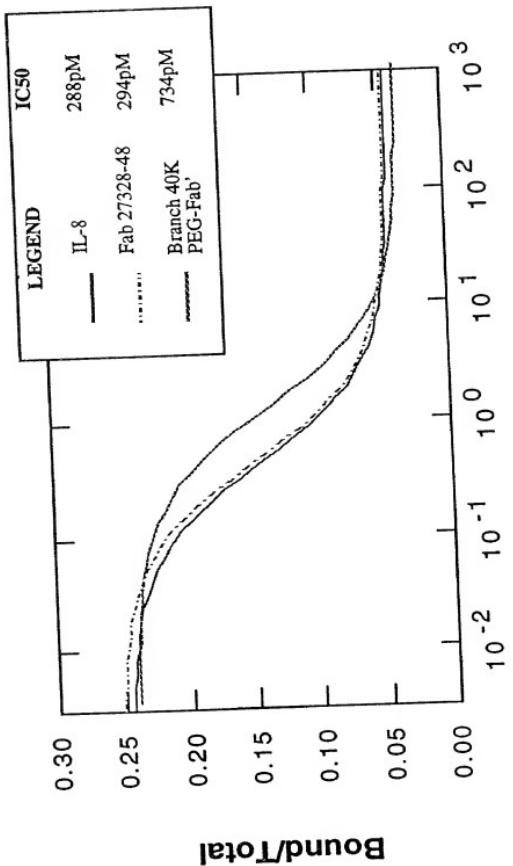


FIG. 54C

FIG. 55A

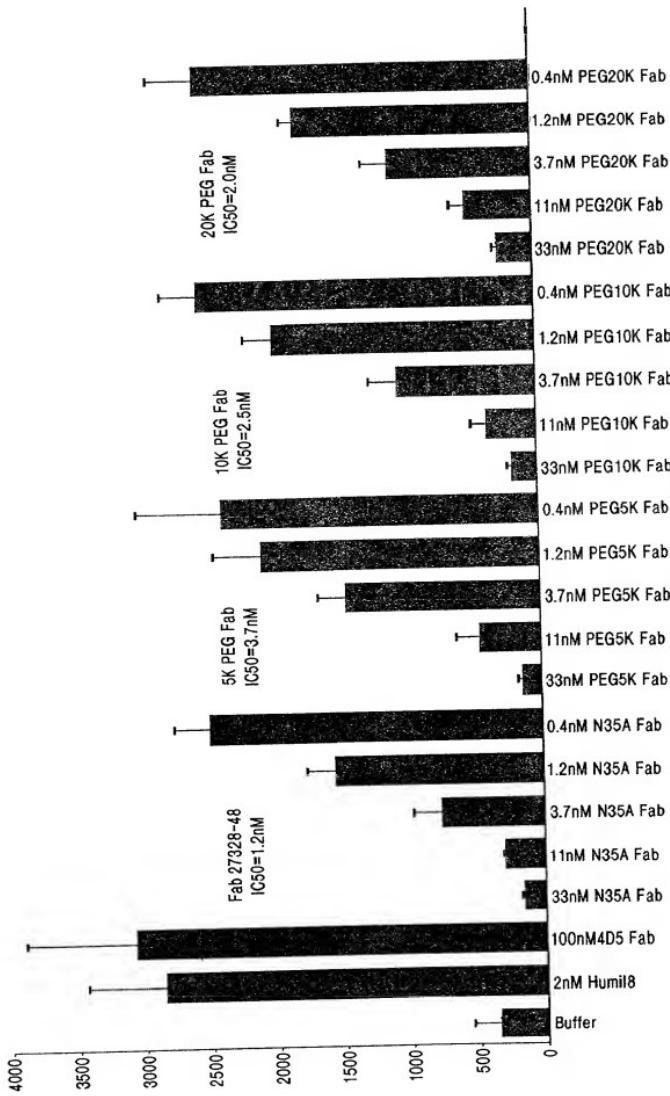


FIG. 5B

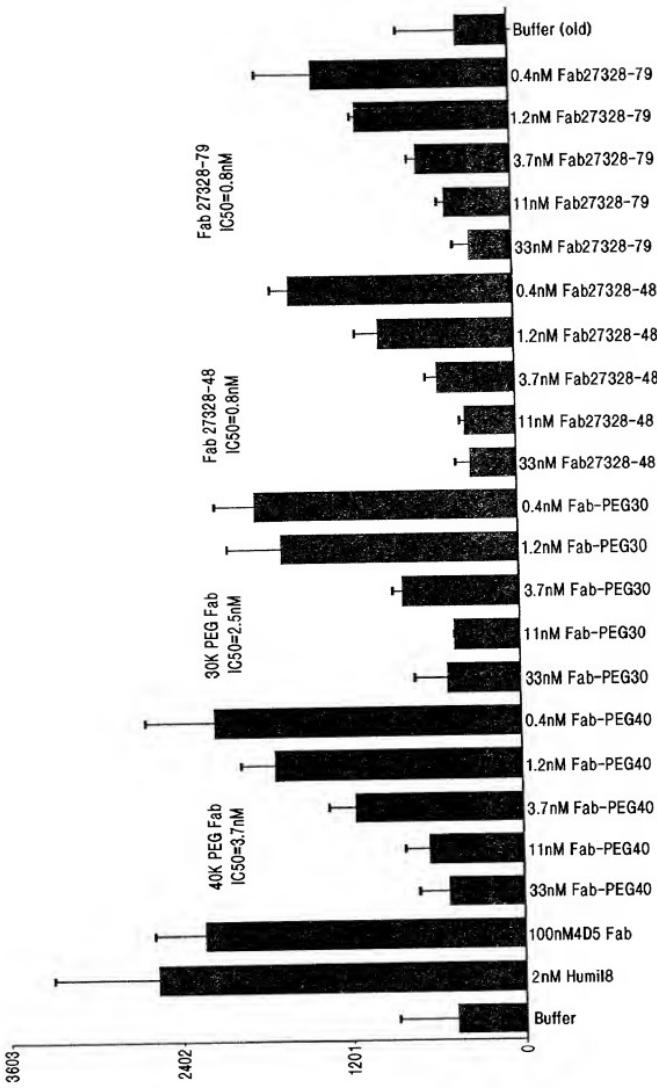
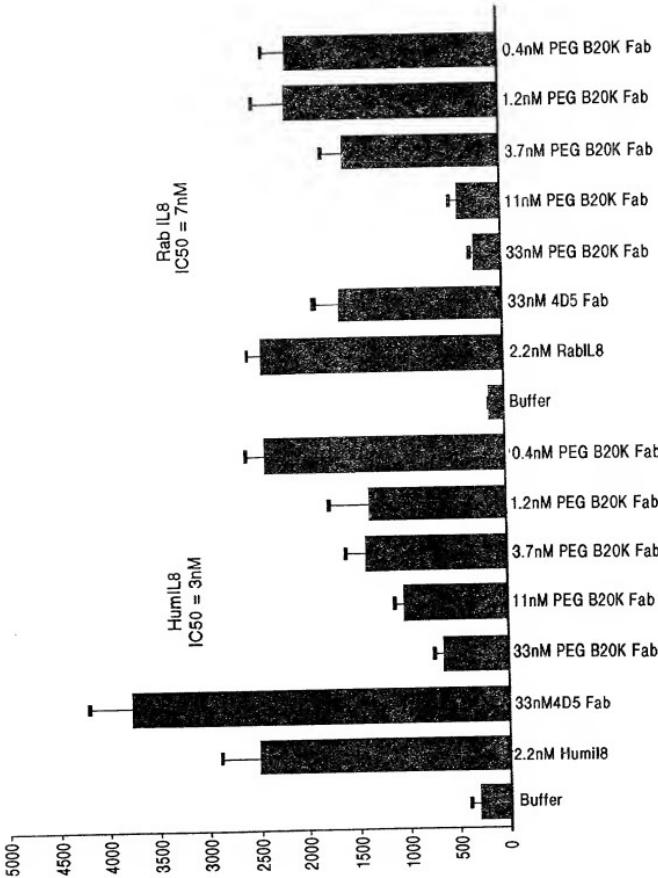


FIG. 55C



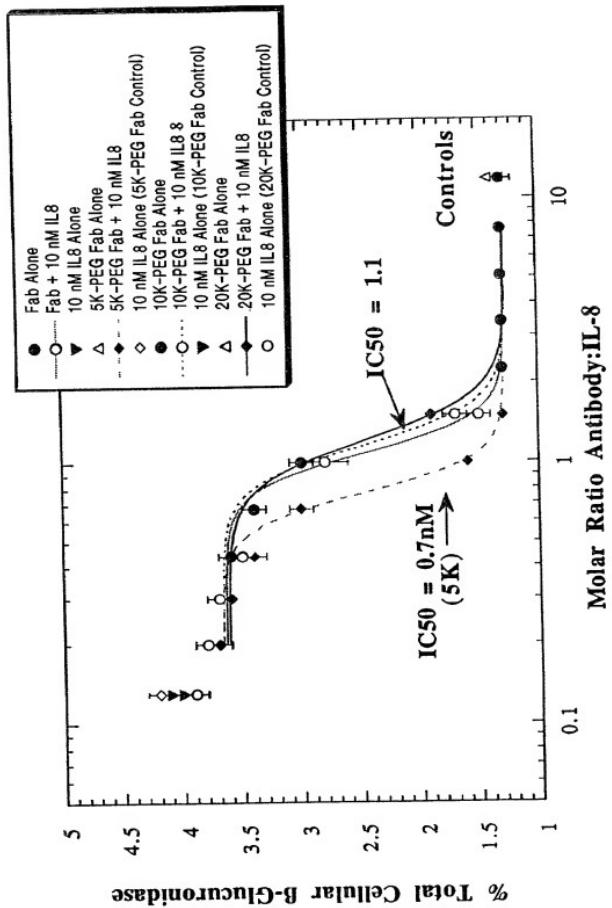
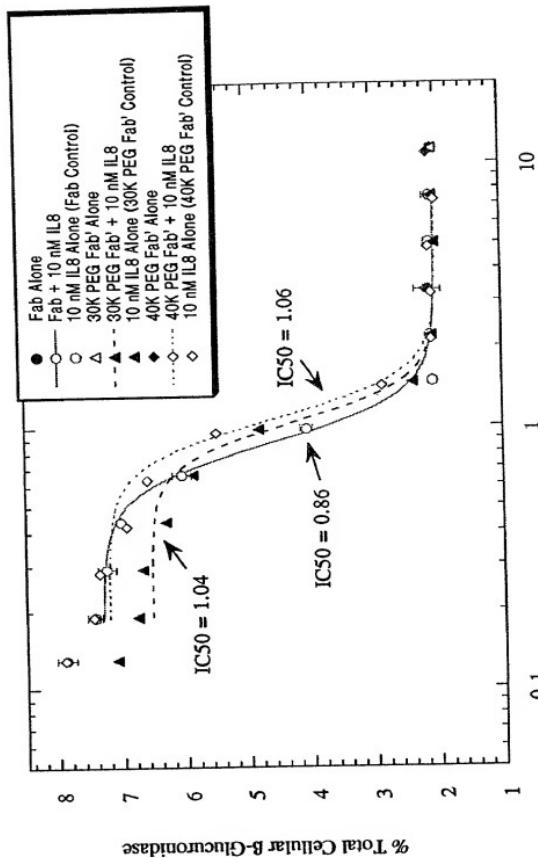


FIG. 56A

FIG. 56B



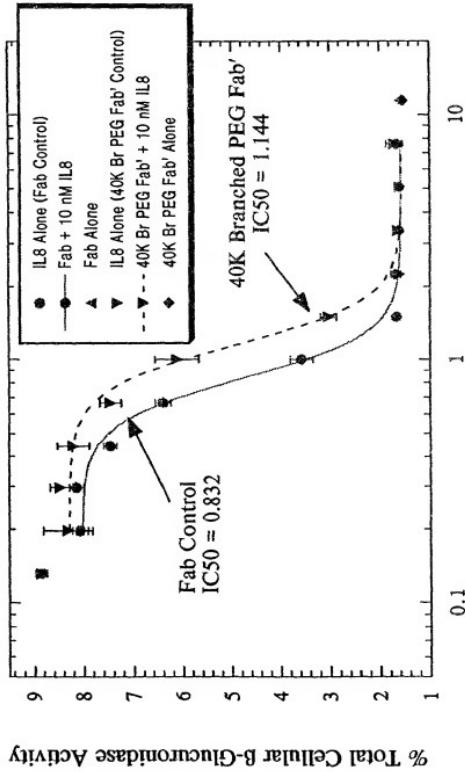


FIG. 56C

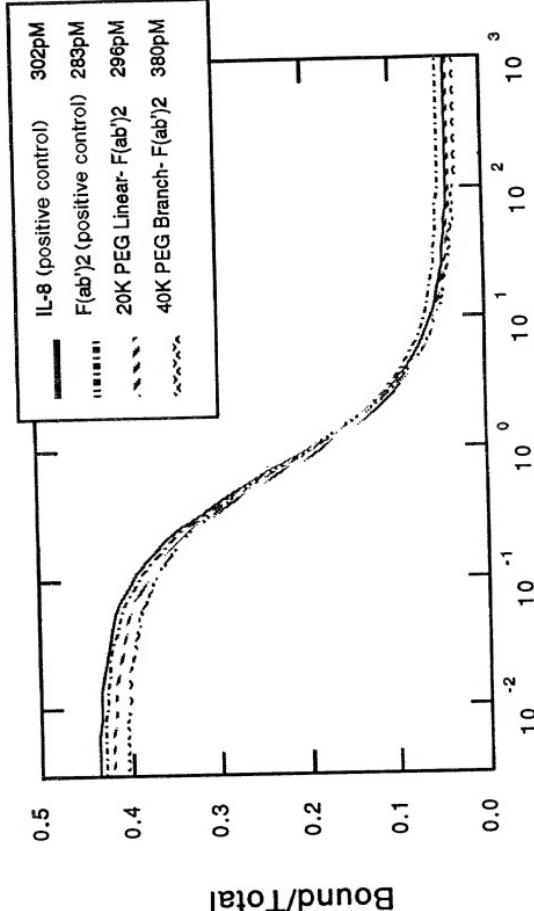


FIG. 57A

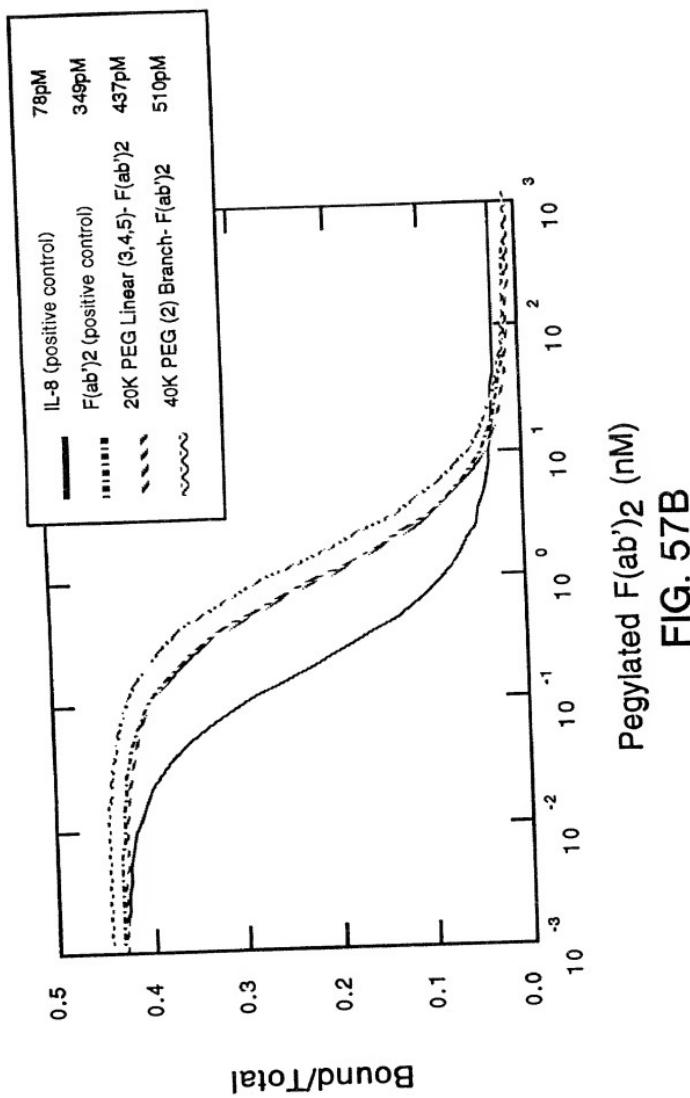


FIG. 57B

FIG. 58A

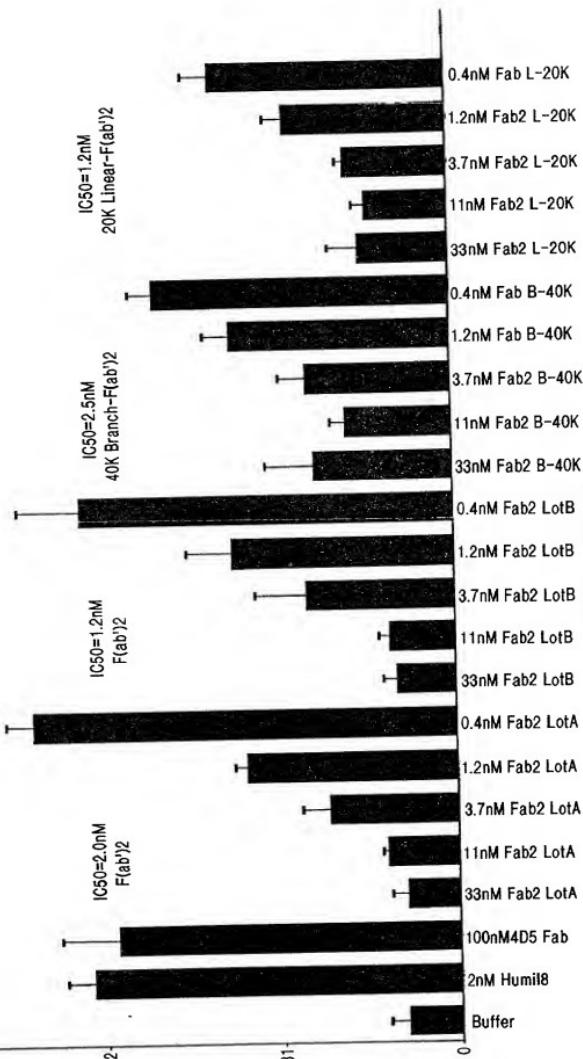


FIG. 58B

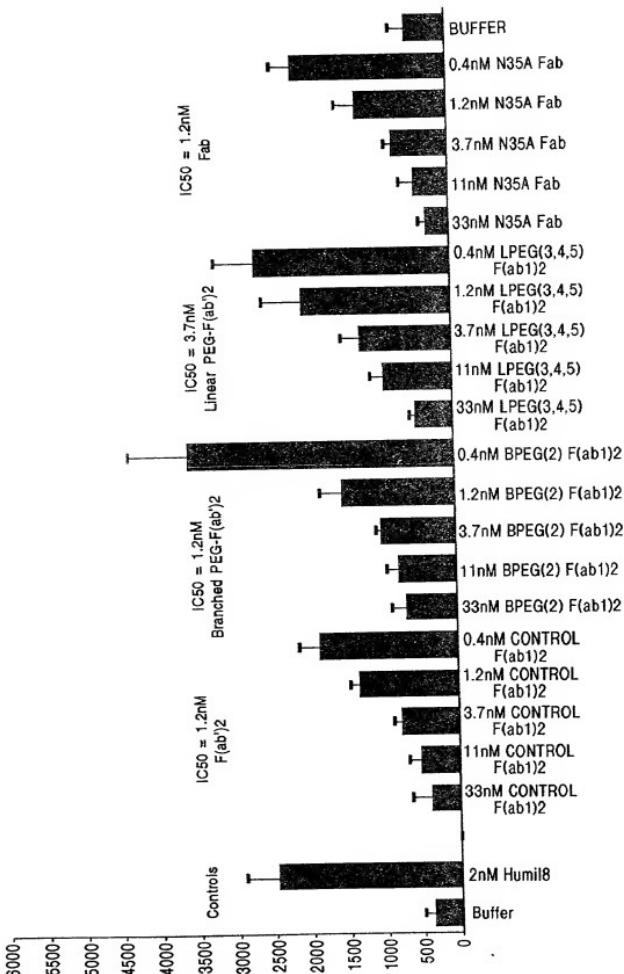


FIG. 59A

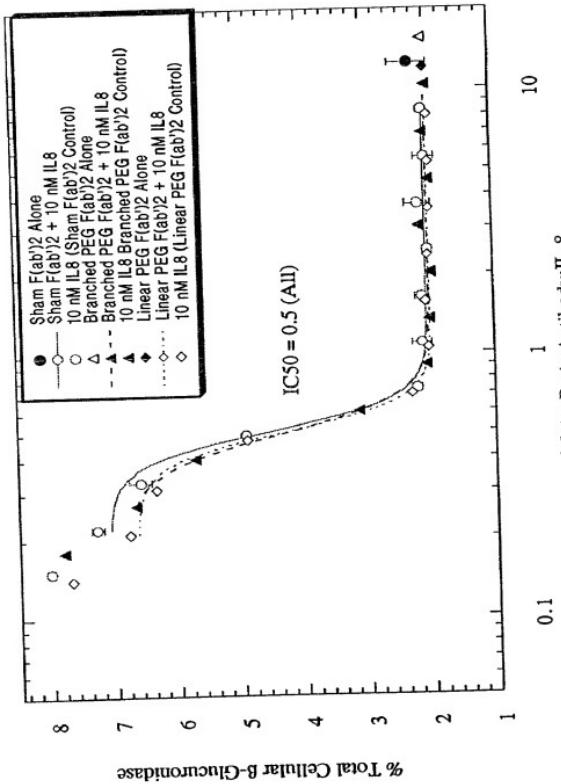
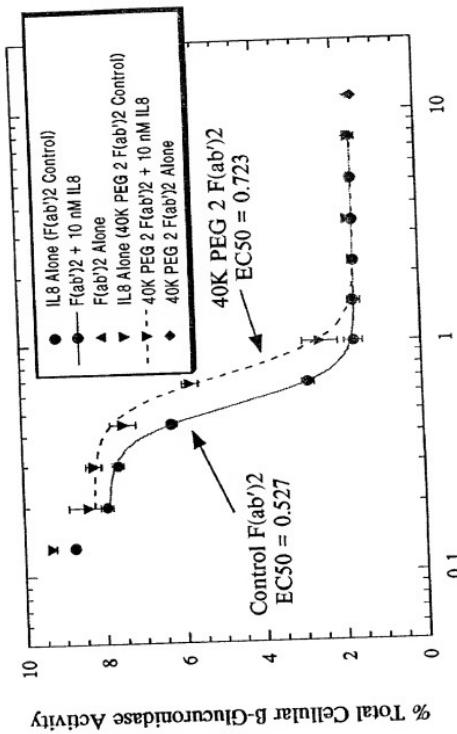
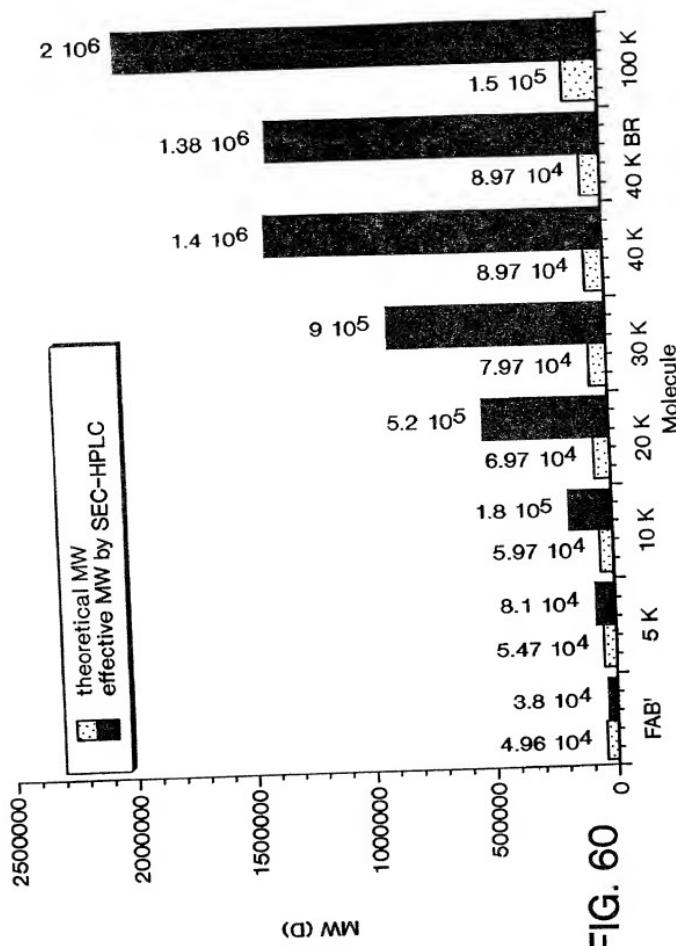


FIG. 59B



70750-85292450



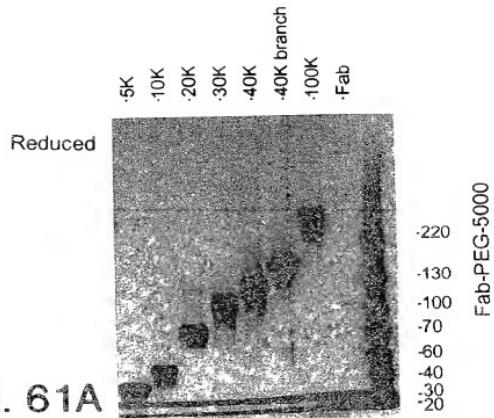


FIG. 61A

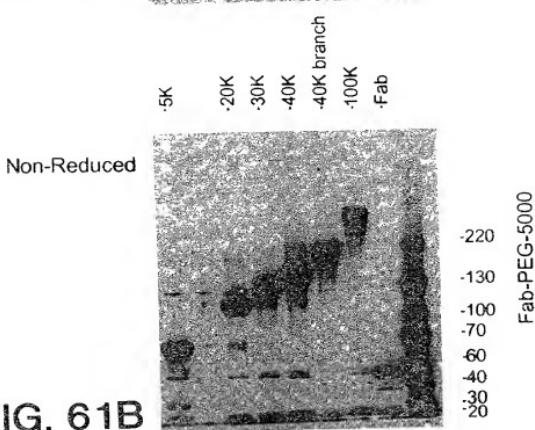


FIG. 61B

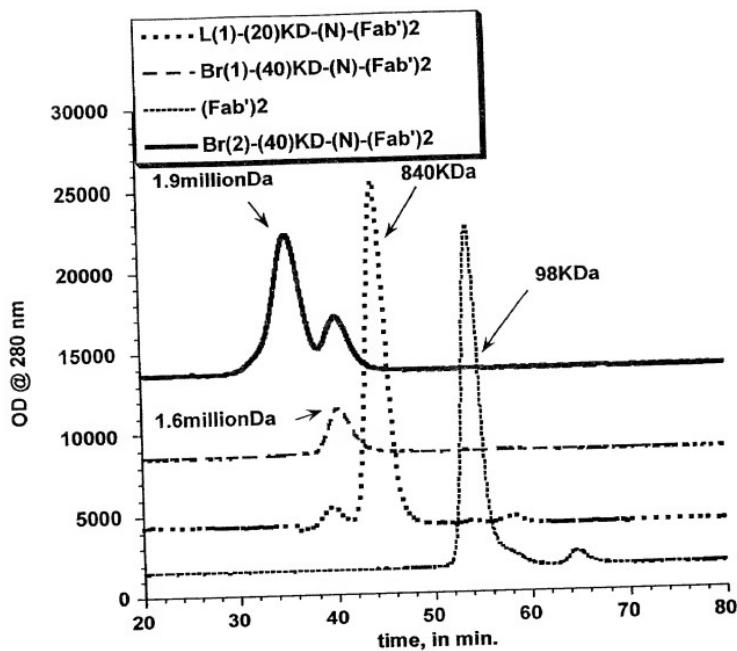


FIG. 62

1973-05-29 260

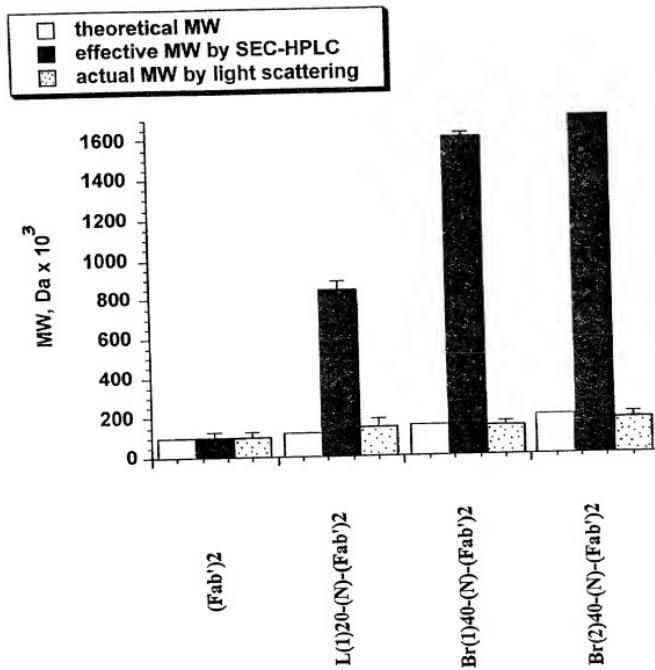


FIG. 63

YOTSEDO 85292465

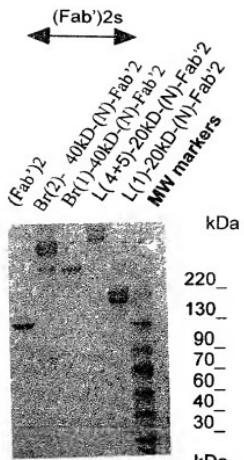


FIG. 64

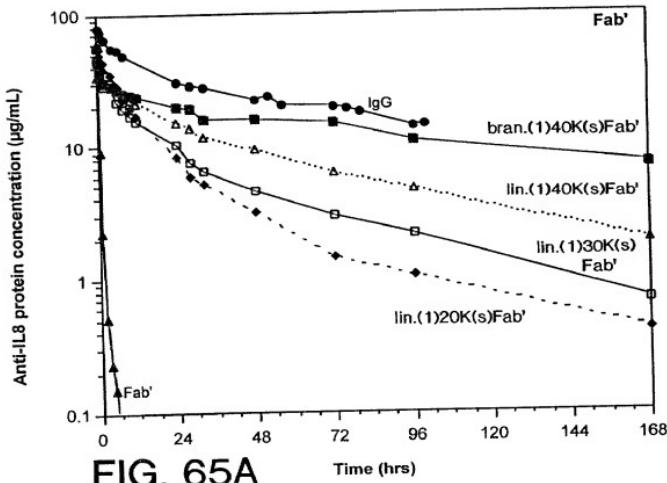


FIG. 65A

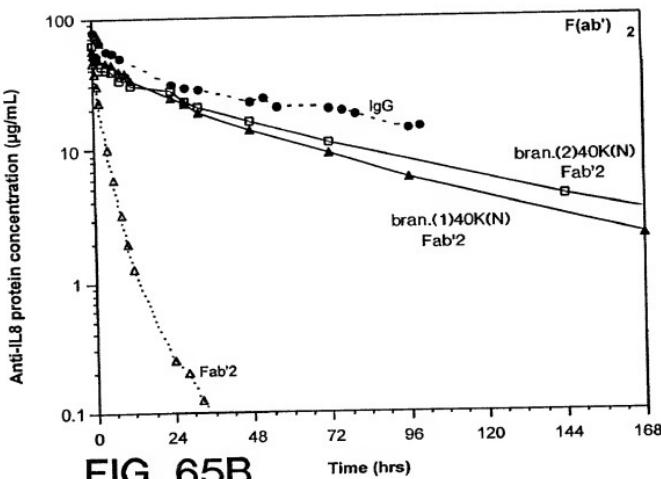


FIG. 65B

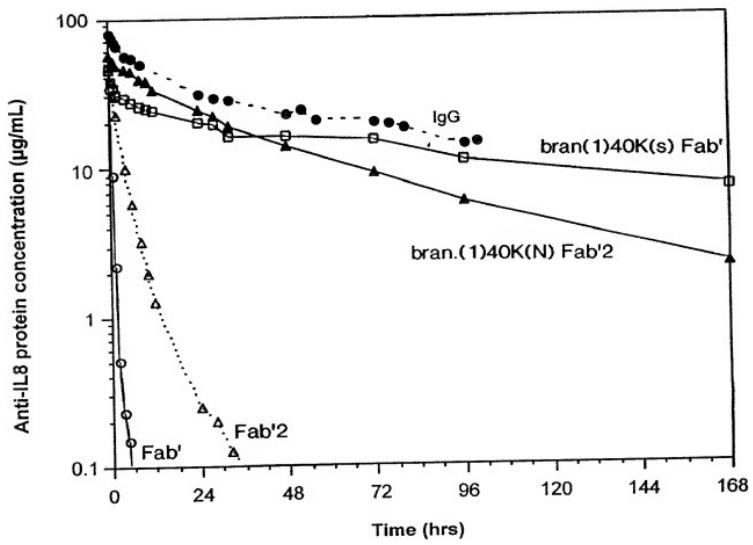


FIG. 66

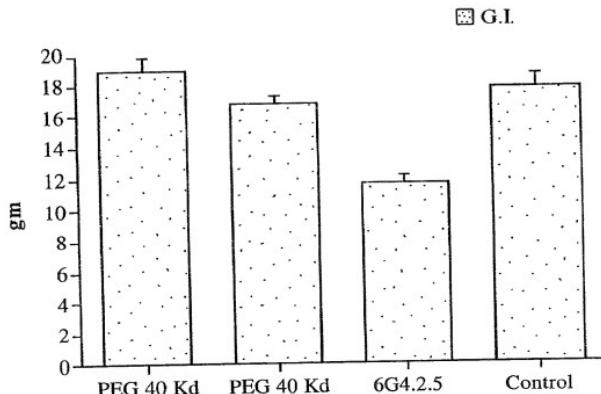


FIG. 67

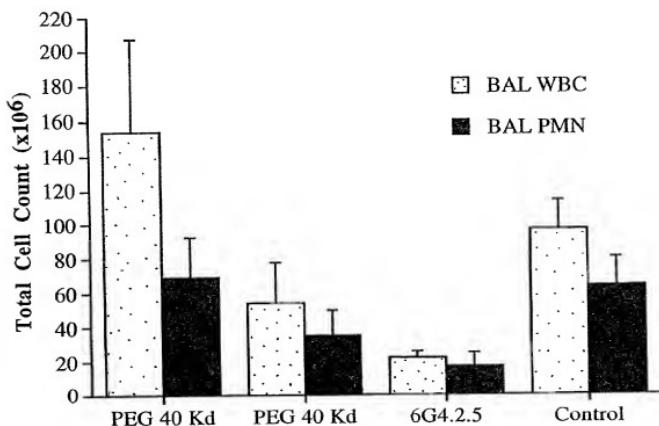


FIG. 68

TOTECO 85293463

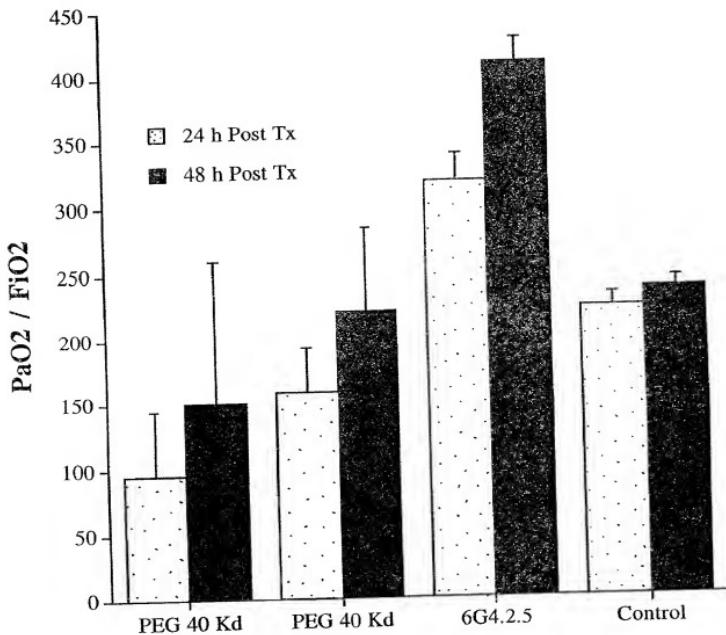


FIG. 69

TESTID = 952927612

Oxygenation in 100% O₂ @24 h Post Anti-IL8 Tx

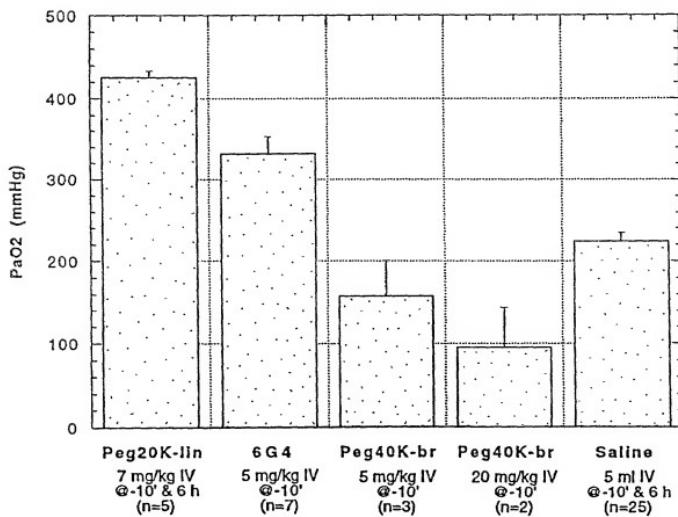


FIG. 70A

2015-08-29 2460

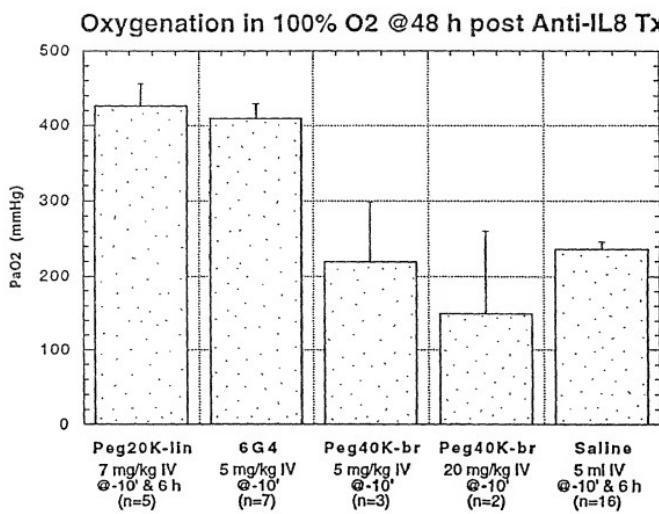


FIG. 70B

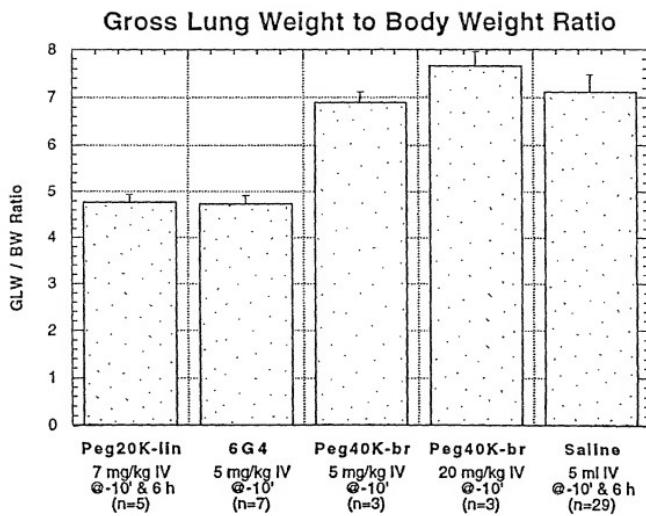


FIG. 70C

2011 EDITION = 95242460

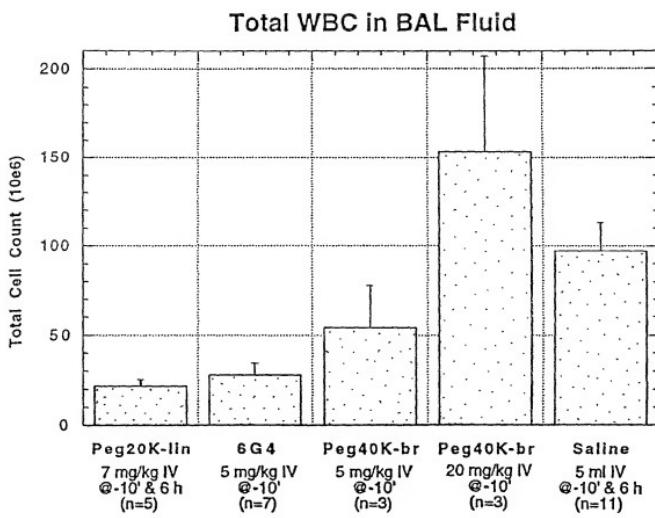


FIG. 70D

107550-85292-Z-51

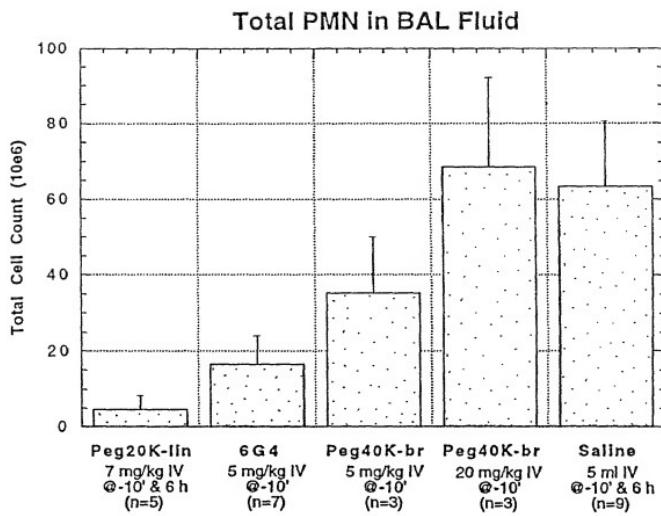
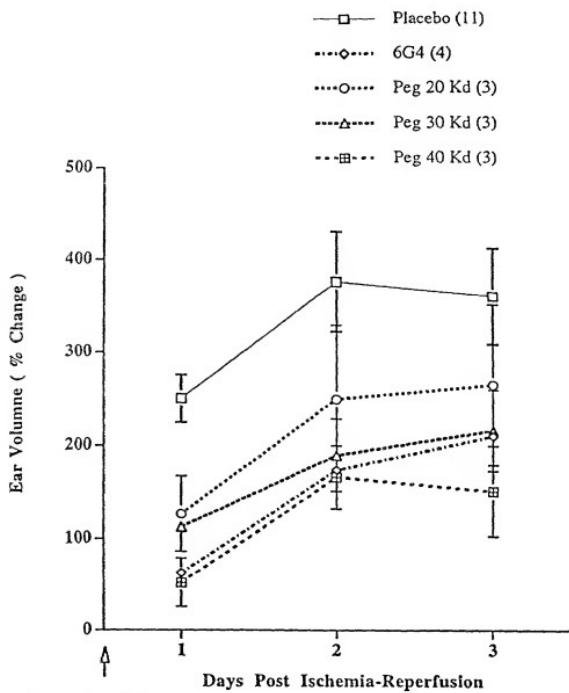


FIG. 70E

307E5D-05292460

The Effect of PEGylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations:
Single Dose (5 mg/kg)
administered IV at time
of reperfusion

FIG. 71